10/ 626,012

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PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
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NEWS 5	DEC 14	2006 MeSH terms loaded for MEDLINE file segment of TOXCENTER
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NEWS 7	DEC 21	IPC search and display fields enhanced in CA/CAplus with the IPC reform
NEWS 8	DEC 23	New IPC8 SEARCH, DISPLAY, and SELECT fields in USPATFULL/ USPAT2
NEWS 9	JAN 13	IPC 8 searching in IFIPAT, IFIUDB, and IFICDB
NEWS 10	JAN 13	New IPC 8 SEARCH, DISPLAY, and SELECT enhancements added to INPADOC
NEWS 11	JAN 17	Pre-1988 INPI data added to MARPAT
NEWS 12	JAN 17	IPC 8 in the WPI family of databases including WPIFV
NEWS 13	JAN 30	Saved answer limit increased
NEWS 14	JAN 31	Monthly current-awareness alert (SDI) frequency added to TULSA
NEWS 15	FEB 21	STN AnaVist, Version 1.1, lets you share your STN AnaVist visualization results
NEWS 16	FEB 22	Status of current WO (PCT) information on STN
NEWS 17	FEB 22	The IPC thesaurus added to additional patent databases on STN
NEWS 18	FEB 22	Updates in EPFULL; IPC 8 enhancements added
NEWS 19	FEB 27	New STN AnaVist pricing effective March 1, 2006

NEWS EXPRESS FEBRUARY 15 CURRENT VERSION FOR WINDOWS IS V8.01a,
CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
AND CURRENT DISCOVER FILE IS DATED 19 DECEMBER 2005.
V8.0 AND V8.01 USERS CAN OBTAIN THE UPGRADE TO V8.01a AT
http://download.cas.org/express/v8.0-Discover/

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NEWS PHONE	Direct Dial and Telecommunication Network Access to STN
NEWS WWW	CAS World Wide Web Site (general information)

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10/ 626,012

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  * * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 16:19:15 ON 28 FEB 2006

=> file reg
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         0.21       0.21

FILE 'REGISTRY' ENTERED AT 16:19:24 ON 28 FEB 2006
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Property values tagged with IC are from the ZIC/VINITI data file
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STRUCTURE FILE UPDATES:   27 FEB 2006  HIGHEST RN 875402-35-0
DICTIONARY FILE UPDATES:  27 FEB 2006  HIGHEST RN 875402-35-0

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TSCA INFORMATION NOW CURRENT THROUGH January 6, 2006

  Please note that search-term pricing does apply when
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*************************************************************************
*                                                                       *
* The CA roles and document type information have been removed from     *
* the IDE default display format and the ED field has been added,       *
* effective March 20, 2005.  A new display format, IDERL, is now        *
* available and contains the CA role and document type information.     *
*                                                                       *
*************************************************************************

Structure search iteration limits have been increased.  See HELP SLIMITS
for details.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document.  For information
on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

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Uploading C:\Program Files\Stnexp\Queries\10626012.str
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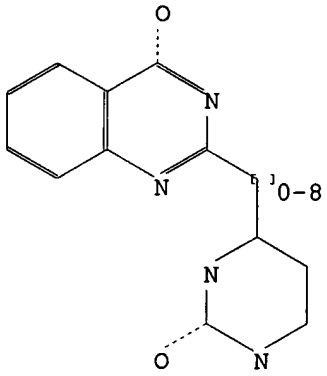
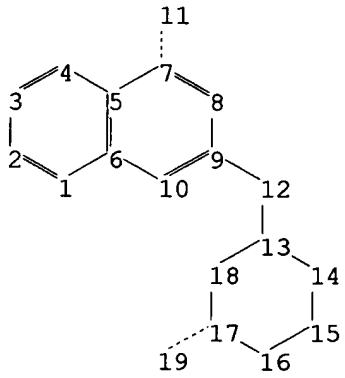


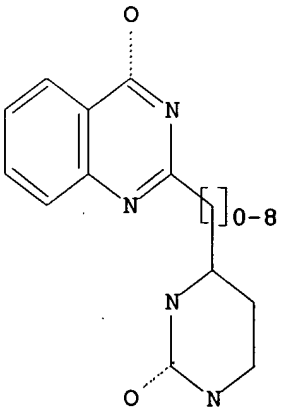


chain nodes :
11 12 19
ring nodes :
1 2 3 4 5 6 7 8 9 10 13 14 15 16 17 18
chain bonds :
7-11 9-12 12-13 17-19
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-10 7-8 8-9 9-10 13-14 13-18 14-15 15-16
16-17 17-18
exact/norm bonds :
7-11 16-17 17-18 17-19
exact bonds :
9-12 12-13 13-14 13-18 14-15 15-16
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-10 7-8 8-9 9-10
isolated ring systems :
containing 1 : 13 :

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:CLASS 12:CLASS 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:CLASS

L1 STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1 STR



Structure attributes must be viewed using STN Express query preparation.

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SAMPLE SEARCH INITIATED 16:19:45 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -        0 TO ITERATE

100.0% PROCESSED         0 ITERATIONS                                0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:            0 TO        0
PROJECTED ANSWERS:               0 TO        0

L2            0 SEA SSS SAM L1

=> s l1 full
FULL SEARCH INITIATED 16:19:54 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -        2 TO ITERATE

100.0% PROCESSED         2 ITERATIONS                                0 ANSWERS
SEARCH TIME: 00.00.01

L3            0 SEA SSS FUL L1

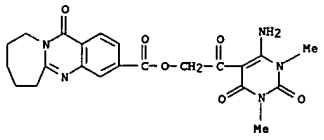
=> s quinazol?
L4       299314 QUINAZOL?

=> s hexahydro and pyrimid?
         552247 HEXAHYDRO
        1108000 PYRIMID?
L5        39615 HEXAHYDRO AND PYRIMID?

=> s l4 and l5
L6           96 L4 AND L5

=> d scan l6
```

L6 96 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN Azepino[2,1-b]quinazoline-3-carboxylic acid, 6,7,8,9,10,12-hexahydro-12-oxo-, 2-(6-amino-1,2,3,4-tetrahydro-1,3-dimethyl-2,4-dioxo-5-pyrimidinyl)-2-oxoethyl ester (9CI)
MF C22 H23 N5 O6



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

10/ 626,012

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=> file hcaplus
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                       182.54     182.75

FILE 'HCAPLUS' ENTERED AT 16:21:39 ON 28 FEB 2006
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FILE COVERS 1907 - 28 Feb 2006  VOL 144 ISS 10
FILE LAST UPDATED: 27 Feb 2006  (20060227/ED)

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 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

=> s l6
L7         2552 L6

=> s l6/thu
           2552 L6
         755953 THU/RL
L8          108 L6/THU
                (L6 (L) THU/RL)

=> d his

     (FILE 'HOME' ENTERED AT 16:19:15 ON 28 FEB 2006)

     FILE 'REGISTRY' ENTERED AT 16:19:24 ON 28 FEB 2006
L1               STRUCTURE UPLOADED
L2             0 S L1 SAMPLE
L3             0 S L1 FULL
L4        299314 S QUINAZOL?
L5         39615 S HEXAHYDRO AND PYRIMID?
L6            96 S L4 AND L5

     FILE 'HCAPLUS' ENTERED AT 16:21:39 ON 28 FEB 2006
L7          2552 S L6
L8           108 S L6/THU

=> d l8 1- ibib abs fhitstr
YOU HAVE REQUESTED DATA FROM 108 ANSWERS - CONTINUE? Y/(N):y
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L8 ANSWER 1 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:1335175 HCAPLUS
DOCUMENT NUMBER: 144:57603
TITLE: Solid orally ingestible formulations of tetrodotoxin
INVENTOR(S): Lin, Weiyang
PATENT ASSIGNEE(S): Can.
SOURCE: U.S. Pat. Appl. Publ., 14 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005282836	A1	20051222	US 2004-872528	20040622
WO 2005123088	A1	20051229	WO 2005-CA973	20050621

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2004-872528 A 20040622

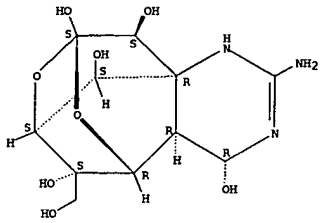
AB The present invention refers to outwardly solid or completely solid oral (or designed to be orally ingested) formulations of tetrodotoxin and/or analogs or derivs. thereof.

IT **4368-28-9**, Tetrodotoxin
RL: **THU (Therapeutic use)**; PYP (Physical process); **THU (Therapeutic use)**; BIOL (Biological study); PROC (Process); USES (Uses)
(solid orally ingestible formulations of tetrodotoxin)

RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L8 ANSWER 1 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)



L8 ANSWER 2 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:1293442 HCAPLUS
DOCUMENT NUMBER: 144:32262
TITLE: Modulation of neurotransmitter activity in neurons
INVENTOR(S): Spitzer, Nicholas C.; Borodinsky, Laura; Root, Cory M.
PATENT ASSIGNEE(S): The Regents of the University of California, USA
SOURCE: PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005115367	A2	20051208	WO 2005-US16851	20050513

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2004-573693P P 20040520

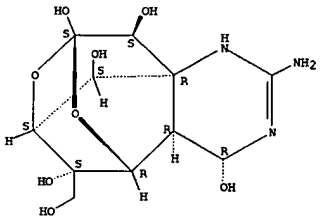
AB This application provides, among others, a method for modulating the neurotransmitter activity of neurons, allowing for the treatment of various psychol. and neurol. disorders and permitting the screening of potential candidate neuromodulators useful in the treatment of various psychol. and neurol. disorders and illnesses. In one embodiment, a method of modulating neurotransmitter activity in a neuron associated with the central nervous system is provided. The method includes contacting the neuron with a stimulatory factor that alters the pattern of Ca2+ spike activity of the neuron. The neuron can be a fully differentiated adult neuron or embryonic neuron. The stimulatory factor can be elec. or chemical The neurotransmitter can be acetylcholine, nitric oxide, histamine, noradrenaline, a bioactive amine, an amino acid or a neuropeptide. Generally, the modulation of neurotransmitter activity comprises altering neurotransmitter expression.

IT **4368-28-9**, Tetrodotoxin
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(modulation of neurotransmitter activity in neurons by stimulatory factor that alters calcium spike activity for treatment of psychol. and neurol. disorders)

RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L8 ANSWER 2 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)



L8 ANSWER 3 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1050483 HCAPLUS
DOCUMENT NUMBER: 143:339667
TITLE: Compositions and methods to increase the effect of a neurotoxin treatment
INVENTOR(S): David, Nathaniel E.
PATENT ASSIGNEE(S): VVII NewCo 2003, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 13 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005214325	A1	20050929	US 2004-810391	20040326
WO 2005091891	A2	20051006	WO 2005-US6300	20050225

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2004-799540 A 20040311
US 2004-799867 A 20040312
US 2004-810391 A 20040326

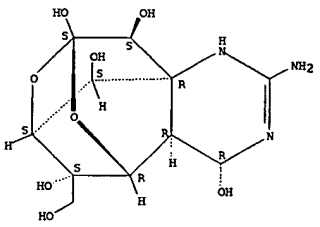
AB The present invention discloses compns. and methods for enhancing the effect (e.g., duration) of a neurotoxin treatment. The compns. herein include neurotoxins and neuron growth inhibitors. Such compns. are administered locally to treat or prevent conditions, such as dermatol. conditions, urol. conditions, thyroid conditions, optical conditions, and neurol. conditions.

IT **4368-28-9**, Tetrodotoxin
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(compns. and methods to increase effect of neurotoxin treatment)

RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L8 ANSWER 3 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)



L8 ANSWER 4 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:647787 HCAPLUS
DOCUMENT NUMBER: 143:399552
TITLE: Differential block of N-propyl derivatives of amitriptyline and doxepin for sciatic nerve block in rats
AUTHOR(S): Gerner, Peter; Luo, Shi Hua; Zhuang, Zhi-Ye; Djalali, Alimorad G.; Zizza, Anthony M.; Myers, Robert R.; Wang, Ging Kuo
CORPORATE SOURCE: Pain Research Center, Department of Anesthesiology, Perioperative and Pain Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, USA
SOURCE: Regional Anesthesia and Pain Medicine (2005), 30(4), 344-350
CODEN: RAPMFX; ISSN: 1098-7339
PUBLISHER: Elsevier Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

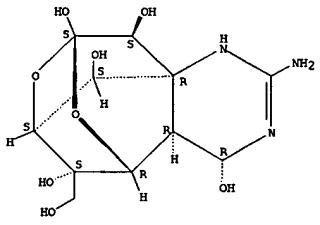
AB The Pr group of ropivacaine (N-propyl-2',6'-pipecoloxylidide hydrochloride) could be responsible for conferring some sensory selectivity to this drug. Thus, adding a Pr group to exptl. local anesthetics (LAs) (e.g., the tricyclic antidepressants amitriptyline and doxepin) to increase sensory selectivity may be useful. We, therefore, synthesized N-Pr amitriptyline and N-Pr doxepin and investigated a potential predominance of sensory/nociceptive block over motor block (differential block) in a rat sciatic nerve block model. In addition, tetrodotoxin (TTX), a naturally occurring Na+ channel blocker, was coinjected to investigate whether it increased block duration. A 0.2-mL test dose of N-Pr amitriptyline and N-Pr doxepin, at a concentration of 1, 2.5, 5, and 10 mM, (alone or in combination with TTX at a concentration of 20 μM) was injected by the subfascial sciatic nerve approach. Motor function and sensory function (nociception) were evaluated by the force a rat's hind limb produced when pushing against a balance and the reaction to pinch, resp. N-Pr amitriptyline and N-Pr doxepin demonstrated prolonged block duration, with N-Pr amitriptyline displaying significant differential block at higher concns. (5 and 10 mM). The combination of either of these drugs with TTX increased the potency as well as the efficacy. Neurotoxicity commenced at concns. of 5 to 10 mM. Detailed histopathol. nerve toxicity evaluations are justified to determine whether N-Pr amitriptyline has potential as a more sensory-selective local anesthetic at lower concns. or as a predominantly sensory-selective neurolytic agent at higher concns.

IT **4368-28-9**, Tetrodotoxin
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(N-Pr amitriptyline, N-Pr doxepin alone or in combination with tetrodotoxin demonstrated prolonged sciatic nerve block duration, N-Pr amitriptyline at higher dose displayed significant differential sciatic nerve block in rat)

RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L8 ANSWER 4 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)



REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 5 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:592616 HCAPLUS
DOCUMENT NUMBER: 144:4602
TITLE: Up-regulation of nNOS and associated increase in nitrergic vasodilation in superior mesenteric arteries in pre-hepatic portal hypertension
AUTHOR(S): Jurzik, Lars; Froh, Matthias; Straub, Rainer H.; Scholmerich, Juergen; Wiest, Reiner
CORPORATE SOURCE: Department of Internal Medicine, University School of Medicine, Regensburg, 93042, Germany
SOURCE: Journal of Hepatology (2005), 43(2), 258-265
CODEN: JOHEEC; ISSN: 0168-8278
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

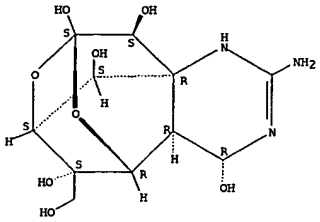
AB Splanchnic arterial vasodilation in portal hypertension has been attributed largely to vascular NO overprodn. Three NO-synthase (NOS) isoforms have been identified of which e(ndothelial)-NOS has been found up-regulated and i(nducible)-NOS not expressed in the splanchnic circulation in portal hypertension. So far, n(euronal)-NOS has not been investigated and hence, the current study evaluates nNOS-expression and nNOS-mediated vasorelaxation in a model of portal vein-ligated rats (PVL). Mesenteric vasculature of PVL and sham rats was evaluated for nNOS-protein (immunohistochem. and Western blotting). In vitro perfused de-endothelialized mesenteric arterial vasculature was pre-constricted with norepinephrine (EC80) and tested for nNOS-mediated vasorelaxation by periarterial nerve stimulation (PNS, 2-12 Hz, 45 V) before and after incubation with the NOS-inhibitor L-NAME (10-4 M). nNOS was localized to the adventitia of the mesenteric arterial tree showing more intense staining and increased protein expression in PVL as compared to sham rats. PNS induced a frequency-dependent vasorelaxation, which was more pronounced in PVL rats. L-NAME abolished this difference in nerval-mediated vasorelaxation, the effect being significantly greater in PVL than in sham animals. Perivascular nNOS-protein expression is enhanced in mesenteric arteries in portal hypertension mediating an increased nerval NO-mediated vasorelaxation. This nNOS-derived NO overprodn. may play an important role in the pathogenesis of arterial vasodilation in portal hypertension.

IT **4368-28-9**, Tetrodotoxin
RL: BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(tetrodotoxin completely blocked periarterial nerve stimulation induced vasorelaxation in mesenteric artery in pre-hepatic portal hypertension rat model)

RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L8 ANSWER 5 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)



REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 6 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:483312 HCAPLUS
DOCUMENT NUMBER: 143:188234
TITLE: Filtration and chromatograph for purifying tetrodotoxin
INVENTOR(S): Liang, Yinghua
PATENT ASSIGNEE(S): Shanghai Huateng Bioengineering Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 7 pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

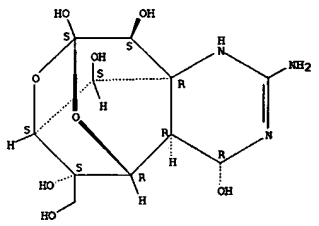
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1425666	A	20030625	CN 2001-142658	20011214
PRIORITY APPLN. INFO.:			CN 2001-142658	20011214

AB Disclosed is a method for purifying tetrodotoxin from globefish. The method comprises cutting the viscera of globefish, milling, press filtering, deactivating to remove protein and grease, filtering through 1-5 μμ filter membrane, 0.1-0.8 μm filter membrane, and then 1-5 nm filter membrane in sequence, purifying on chromatog. column, and crystallizing The purified tetrodotoxin may be used as sedative or analgesic, and is especially useful for reducing malignancy pain and drug withdrawal syndrome.

IT **4368-28-9P**, Tetrodotoxin
RL: BSU (Biological study, unclassified); PUR (Purification or recovery); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(filtration and chromatograph for purifying tetrodotoxin for use as sedative and analgesic)

RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L8 ANSWER 7 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:462110 HCAPLUS
DOCUMENT NUMBER: 143:76424
TITLE: Immunologic protection of anti-tetrodotoxin vaccines against lethal activities of oral tetrodotoxin challenge in mice
AUTHOR(S): Xu, Qin-Hui; Zhao, Xiu-Nan; Wei, Chang-Hua; Rong, Kang-Tai
CORPORATE SOURCE: Beijing Institute of Pharmacology and Toxicology, Beijing, 100850, Peop. Rep. China
SOURCE: International Immunopharmacology (2005), 5(7-8), 1213-1224
CODEN: IINMBA; ISSN: 1567-5769
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

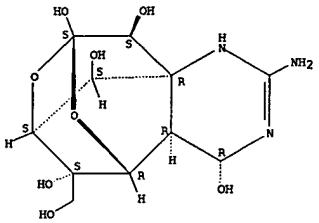
AB Tetrodotoxin (TTX) is a high toxic small mol. neurotoxin. Haptenic vaccine for TTX was investigated and the carrier proteins were compared. TTX was conjugated to Tachypleus tridentatus hemocyanin (TTH) and tetanus toxoid (TT) via formaldehyde to form the artificial antigen TTX-TTH and TTX-TT. BALB/c mice were immunized with the artificial antigen, the TTX-specific antibody response were detected. The immunized animals were intragastrically challenged with increasing doses of TTX repeatedly. The mice which exposed to TTX in doses of 600, 630, 800, 1200, 1500, 2000 and 2400 μg/kg survived at rates of 100, 100, 90, 90, 80, 50 and 20%, with a LD50 value of 2020 μg/kg for TTH-TTX vaccine, and of 100%, 90.9%, 90.9%, 90.9%, 63.6%, 27.3% and 0%, with a LD50 value of 1410 μg/kg for TT-TTX vaccine, resp. All control mice inoculated with carrier protein TTH or TT uniformly died of a dose of 600 μg/kg TTX i.g. challenge. Animals immunized with vaccines could antagonize repeated TTX challenge, half of them surviving about 6 mg/kg, and a few being able to bear a maximal accumulative dose as high as approx. 9 mg/kg of TTX challenges within eight months. The TTH-TTX vaccine was of the more excellent in protective effect from TTX oral intoxication, mainly resulted from the higher antibody affinity than that from TT-TTX vaccine. The present study for the first time demonstrated that the anti-TTX exptl. vaccines would high effectively protect animal from multiple, oral TTX intoxication. Immunoprophylaxis would be the hopeful means against TTX poisoning.

IT **4368-28-9**, Tetrodotoxin
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(conjugated with hemocyanin or tetanus toxoid; protection of anti-tetrodotoxin vaccines against lethal activities of oral tetrodotoxin challenge in mice)

RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L8 ANSWER 7 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)



REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 8 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:369235 HCAPLUS
DOCUMENT NUMBER: 142:404275
TITLE: Compositions and methods for enhancing cognitive function and synaptic plasticity
INVENTOR(S): Liu, Guosong; Slutsky, Inna
PATENT ASSIGNEE(S): Massachusetts Institute of Technology, USA
SOURCE: PCT Int. Appl., 145 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005037215	A2	20050428	WO 2004-US33971	20041014

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-510945P P 20031014

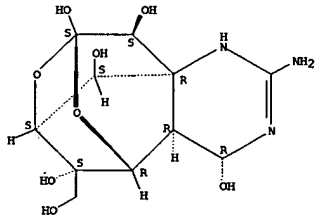
AB The invention provides compns. and methods for enhancing cognitive function and synaptic plasticity. According to the method, Ca++ influx into excitatory neurons (nerve cells) is decreased by treatment with a number of different agents including divalent cations (e.g., Mg++), GABAB agonists, GABAA agonists, calcium channel blockers, and/or compds. that decrease action potential firing such as sodium channel blockers. Decreasing Ca++ influx results in increased synaptic plasticity and enhanced cognitive function. In particular, decreasing Ca++ influx associated with uncorrelated neural activity results in long-lasting increases in synaptic plasticity and cognitive function. This is achieved by administration of agents that cause a voltage-dependent block of NMDA receptors (e.g., divalent cations such as Mg++) or by administration of GABAB agonists such as baclofen. The invention further provides screening methods useful in identifying compds. that enhance synaptic plasticity and cognitive function.

IT **4368-28-9**, TTX
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(compns. and methods for enhancing cognitive function and synaptic plasticity)

RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L8 ANSWER 8 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)



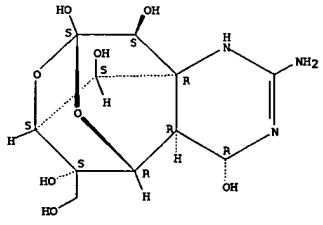
L8 ANSWER 9 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:322057 HCAPLUS
DOCUMENT NUMBER: 143:344497
TITLE: Myocytes from congenital myotonic dystrophy display abnormal Na+ channel activities
AUTHOR(S): Bernareggi, Annalisa; Furling, Denis; Mouly, Vincent; Ruzzier, Fabio; Sciancalepore, Marina
CORPORATE SOURCE: Department of Physiology and Pathology, University of Trieste, Trieste, 34127, Italy
SOURCE: Muscle & Nerve (2005), 31(4), 506-509
CODEN: MUNEDE; ISSN: 0148-639X
PUBLISHER: John Wiley & Sons, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Na+ currents were measured in myocytes from a fetus with congenital myotonic dystrophy type 1 (DM1) using the patch-clamp whole-cell technique. Steady-state activation and inactivation properties of Na+ channels were not substantially different between these cells and age-matched control cells. However, a decrease in Na+ channel d. and a faster rate of recovery from inactivation were found in myocytes from congenital DM1 suggesting that changes in functional Na+ channels may affect cell excitability of muscle cells of patients with this disorder.

IT **4368-28-9**, Tetrodotoxin
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(tetrodotoxin reduced Na+ c.d. and TTX-resistant inward current disappeared when extracellular NaCl was replaced by N-methyl-D-glucamine in congenital myotonic dystrophy type I human myocyte)

RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 10 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:214987 HCAPLUS
DOCUMENT NUMBER: 143:264135
TITLE: Sodium channels and neuropathic pain
AUTHOR(S): Chung, Jin Mo; Chung, Kyungsoon
CORPORATE SOURCE: Department of Neuroscience & Cell Biology, University of Texas Medical Branch, Galveston, TX, 77555-1069, USA
SOURCE: Novartis Foundation Symposium (2004), 261(Pathological Pain), 19-31
CODEN: NFSYF7; ISSN: 1528-2511
PUBLISHER: John Wiley & Sons Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

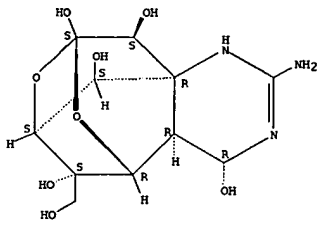
AB A review. Although it has long been known that sodium channels play an important role in the generation of abnormal neuronal activity and neuropathic pain, it is only recently that we have begun to understand the subtypes of sodium channels which are particularly important in neuropathic pain. Many of the identified subtypes of sodium channels are localized in dorsal root ganglion (DRG) neurons. Based on their sensitivity to tetrodotoxin (TTX), these sodium channels are classified as TTX-sensitive (TTXs) or TTX-resistant (TTXr) subtypes. In in vitro electrophysiol. expts., ectopic discharges arising from DRG neurons with injured axons are blocked by TTX at doses that are too low to block TTXr subtypes. Furthermore, the same low doses of TTX applied to the DRG of the injured segment in neuropathic rats significantly reduce pain behaviors. These data suggest that TTXs subtypes of sodium channels are playing an important role in the generation of both ectopic discharges and neuropathic pain. Anal. of mRNA of the TTXs subtypes of sodium channels in the DRG after spinal nerve ligation showed that Nav1.3 (Type III) and Nax (NaG) are the only two subtypes that are up-regulated, suggesting their potentially important role in ectopic discharge and neuropathic pain generation.

IT **4368-28-9**, Tetrodotoxin
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(TTX subtypes of Na channels play role in generation of ectopic discharge and neuropathic pain, Nav1.3 (Type III) and Nax (NaG) are two subtypes that are up-regulated suggesting their importance in pain generation in DRG neurons in rat)

RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L8 ANSWER 10 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 11 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:85697 HCAPLUS
DOCUMENT NUMBER: 142:360773
TITLE: Drug-abstaining and analgesic medical formulation and its preparation
INVENTOR(S): Lin, Wenhan
PATENT ASSIGNEE(S): Wang, Kaiye, Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 7 pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1485039	A	20040331	CN 2002-131020	20020924

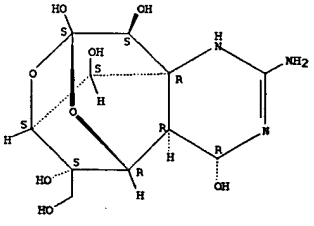
PRIORITY APPLN. INFO.: CN 2002-131020 20020924

AB The drug-abstaining and analgesic injection is composed of tetrodotoxin 0.1-20.0 μg, citric acid 0.5-100 μg, and water 1 mL. Tetrodotoxin is isolated by beating ovary, viscus, and skin of globefish, vacuum concentrating the supernatant, dissolving the residual solid in 20% acetic acid solution, precipitating with ethanol, vacuum concentrating the supernatant to obtain crude tetrodotoxin, and purifying on C18 column.

IT **4368-28-9**, Tetrodotoxin
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(drug-abstaining and analgesic medical formulation and its preparation)

RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L8 ANSWER 12 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN

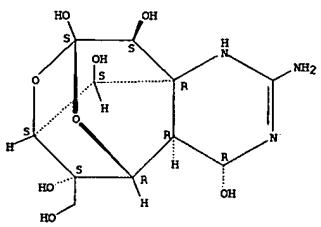
ACCESSION NUMBER: 2005:64531 HCAPLUS
DOCUMENT NUMBER: 142:384963
TITLE: A microcapsule technique for long-term conduction block of the sciatic nerve by tetrodotoxin
AUTHOR(S): Martinov, Vladimir N.; Nja, Arild
CORPORATE SOURCE: Department of Physiology, Institute for Basic Medical Sciences, University of Oslo, Oslo, N-0317, Norway
SOURCE: Journal of Neuroscience Methods (2005), 141(2), 199-205
CODEN: JNMEDT; ISSN: 0165-0270
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Tetrodotoxin (TTX) is a selective blocker of voltage-gated Na+ channels that is used to block action potentials in vitro and in vivo. Maintaining a sufficiently high local concentration of TTX in vivo to block conduction in a peripheral nerve is tech. demanding and carries a risk of systemic toxicity. We report that slow diffusion of TTX out of a microcapsule (glass capillary) inserted beneath the epineurium of the sciatic nerve, with a loose cuff around the nerve, combines high blocking efficacy with low systemic toxicity in rats and mice. The local anesthesia and motor paralysis was stable for at least 4-6 wk. The conduction block was reversible and did not cause any obvious nerve injury. Low cost and simple surgical implementation make this new system an interesting alternative to existing long-term drug delivery methods.

IT **4368-28-9**, Tetrodotoxin
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(tetrodotoxin via microcapsule technique inserted beneath epineurium of sciatic nerve reversibly blocked impulse conduction and did not cause nerve injury, showed low systemic toxicity in mouse and rat)

RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 12 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)

L8 ANSWER 13 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:55070 HCAPLUS
DOCUMENT NUMBER: 142:141258
TITLE: Stable tetrodotoxin freeze drying medicinal formulation containing disaccharides or polysaccharides as stabilizer
INVENTOR(S): Zhang, Xiao; Kang, Yuhong; Huang, Xiaoyan
PATENT ASSIGNEE(S): Nanning Maple Leaf Pharmaceutical Co., Ltd., Peop. Rep. China
SOURCE: PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005004874	A1	20050120	WO 2004-CN736	20040702
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CN 1568999	A	20050126	CN 2003-146020	20030714
US 2005020610	A1	20050127	US 2004-890279	20040714

PRIORITY APPLN. INFO.: CN 2003-146020 A 20030714

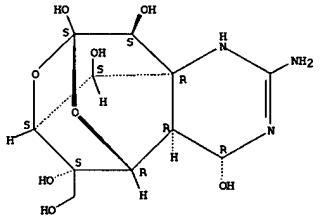
AB Disclosure is a freeze drying preparation for injection containing in each dose 0.5 to 60μg tetrodotoxin or the analogs thereof, which has good stability and low toxicity, and can be stored at room temp for a long period of time. Said preparation also contains compds. which can reduce C-4 hydroxy activity of tetrodotoxin or the analogs thereof, such as glucosidic linkage containing compds. selected from any one of disaccharides, polysaccharide, the derivs. thereof or their mixture, and acid solubilizer which improves dissolving of tetrodotoxin or the analogs thereof. For example, an injection solution containing tetrodotoxin 3, lactose 3,000 (as stabilizer), citric acid 0.012 mg was frozen dried and showed improved stability comparing with fructose as stabilizer.

IT **4368-28-9**, Tetrodotoxin
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(tetrodotoxin freeze drying injections containing disaccharides or polysaccharides as stabilizers and acids as solubilizers for improved stability)

RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L8 ANSWER 13 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 14 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:1045477 HCAPLUS
DOCUMENT NUMBER: 142:469133
TITLE: Tetrodotoxin conjugate and its medical composition
INVENTOR(S): Xu, Qinhui; Rong, Kangtai
PATENT ASSIGNEE(S): Institute of Toxic Medicine, Academy of Military Medical Science of PLA, Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 18 pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1465403	A	20040107	CN 2002-123142	20020619

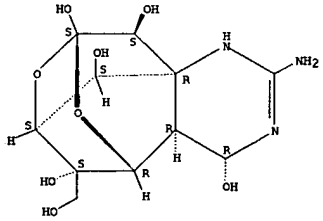
PRIORITY APPLN. INFO.: CN 2002-123142 20020619

AB The conjugate of tetrodotoxin (TTX) with carrier (such as hemocyanin of limulus, tetanus toxoid, or their fragments) is prepared by coupling TTX with hemocyanin (at a molar ratio of 250-7.0) in the presence of linker (1-2%; such as formaldehyde or glutaraldehyde) at 30°C for 72 h, and then dialyzing at 4°C to remove free toxin. The conjugate may be used to prepare monoclonal antibody, antiserum, or antitoxin as anti-TTX vaccine, also as immunol. affinity chromatog. reagent for purifying anti-TTX antibody, as immunoassay reagent for detecting TTX, further as the analytic reagent for studying electrophysiol. and pharmacokinetics of TTX, etc.

IT **4368-28-9**, Tetrodotoxin
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); **THU (Therapeutic use)**; BIOL (Biological study); PROC (Process); USES (Uses)
(tetrodotoxin conjugate and its medical composition)

RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L8 ANSWER 15 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:1022045 HCAPLUS
DOCUMENT NUMBER: 142:190998
TITLE: Propylene glycol increases cytosolic free calcium in rat cerebrocortical synaptosomes
AUTHOR(S): Satoh, Eiki; Murakami, Kei; Nishimura, Masakazu
CORPORATE SOURCE: Department of Pathobiological Science, Obihiro University of Agriculture and Veterinary Medicine, Obihiro, Japan
SOURCE: International Journal of Neuroscience (2004), 114(5), 587-596
CODEN: IJNUB7; ISSN: 0020-7454
PUBLISHER: Taylor & Francis, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

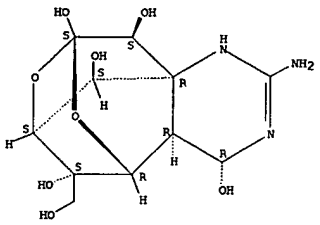
AB In these studies, the authors investigated the effect of propylene glycol (PG) on the cytosolic free Ca2+ concentration ([Ca2+]i) in rat cerebrocortical synaptosomes using the fluorescent Ca2+ indicator fura-2. PG (0.5-5% volume/volume) increased [Ca2+]i in a concentration-dependent manner. The PG-induced increase in [Ca2+]i seas inhibited approx. 50% by the omission of extracellular Ca2+ or the addition of Ni2+ (100 μM). Decrease of extracellular Na+ (6.2 mM) or addition of tetrodotoxin (1 μM), verapamil (10 μM), nifedipine (10 μM), ω-agatoxin IVA (200 nM), ω-conotoxin GVIA (1 μM), or ω-conotoxin MVIIC (1 μM) had no effect on the increase in [Ca2+]i. Also, addition of TMB-8 (100 μM), ryanodine (50 μM) or thapsigargin (1 μM) did not modify the increase in [Ca2+]i in the absence of extracellular Ca2+. These results suggest that PG increases [Ca2+]i in rat cerebrocortical synaprosomes by both stimulating Ca2+ entry through a Ni2+-sensitive pathway and releasing Ca2+ from TMB-8-, ryanodine- and thapsigargin-insensitive Ca2+ stores.

IT **4368-28-9**, Tetrodotoxin
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(low Na+ in resting [Ca2+]i was higher than in presence of NaCl and voltage-dependent Na+ channel blocker tetrodotoxin had no effect in rat cerebrocortical synaptosomes)

RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L8 ANSWER 15 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)



REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 16 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:969536 HCAPLUS
DOCUMENT NUMBER: 142:225714
TITLE: Therapeutic agent for treatment of hemorrhoids using roe of globefish and production
INVENTOR(S): Lim, Gap Man
PATENT ASSIGNEE(S): S. Korea
SOURCE: Repub. Korean Kongkae Taeho Kongbo, No pp. given
CODEN: KRXXA7
DOCUMENT TYPE: Patent
LANGUAGE: Korean
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

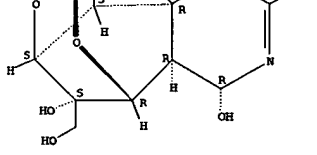
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
KR 2002064807	A	20020810	KR 2001-5223	20010203
PRIORITY APPLN. INFO.:			KR 2001-5223	20010203

AB A process of preparing a therapeutic agent for hemorrhoids by heating the roe of a globefish at a specified temperature and then mixing sodium chloride is provided. The therapeutic agent for hemorrhoids is burned with alc. and a portion of hemorrhoids is exposed thereto. The roe of a globefish is heated at 0 to 30° for 50 to 150 days, ground and mixed with sodium chloride to produce a therapeutic agent for hemorrhoids containing tetrodotoxin.

IT **4368-28-9**, Tetrodotoxin
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(therapeutic agent for treatment of hemorrhoids using roe of globefish)

RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L8 ANSWER 17 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:943433 HCAPLUS
DOCUMENT NUMBER: 142:204664
TITLE: Pharmaceutical composition for treatment of cancer containing globefish extract
INVENTOR(S): Kim, Ik Soo
PATENT ASSIGNEE(S): S. Korea
SOURCE: Repub. Korean Kongkae Taeho Kongbo, No pp. given
CODEN: KRXXA7
DOCUMENT TYPE: Patent
LANGUAGE: Korean
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

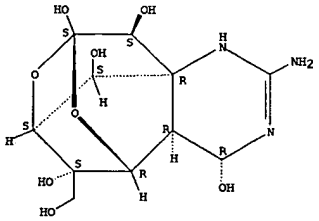
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
KR 2002091641	A	20021206	KR 2001-30481	20010531
PRIORITY APPLN. INFO.:			KR 2001-30481	20010531

AB A pharmaceutical composition containing a globefish extract which contains Tetrodotoxin as a main component is provided which has an advantage of obtaining analgesic activity while treating cancer when administered to a patient who suffers from cancer pains. The pharmaceutical composition comprises a globefish extract as an active ingredient, an anticancer agent containing one or more selected from the group consisting of 5-fluorouracil, methotrexate, adriamycin and taxol and a pharmaceutically acceptable additive containing one of a stabilizer, favoring agent and corrigent. The ovary of a globefish is extracted in water at 100°C for 24h and then centrifuged after removing suspended solids.

IT **4368-28-9**, Tetrodotoxin
RL: NPO (Natural product occurrence); **THU (Therapeutic use)**; BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(antitumor compns. containing anticancer drugs and tetrodotoxin from globefish ovary as analgesics)

RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



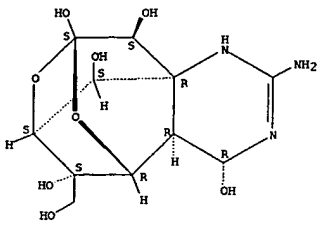
L8 ANSWER 18 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:927018 HCAPLUS
DOCUMENT NUMBER: 141:388733
TITLE: Compositions of a cyclooxygenase-2 selective inhibitor and a sodium ion channel blocker for the treatment of central nervous system damage
INVENTOR(S): Stephenson, Diane T.; Taylor, Duncan P.
PATENT ASSIGNEE(S): Pharmacia Corporation, USA
SOURCE: PCT Int. Appl., 164 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004093811	A2	20041104	WO 2004-US12383	20040421
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 20042249 40	A1	20041111	US 2004-829009	20040421
PRIORITY APPLN. INFO.:			US 2003-464499P P	20030422
			US 2003-464830P P	20030423

OTHER SOURCE(S): MARPAT 141:388733
AB The invention provides compns. and methods for the treatment of central nervous system damage in a subject. More particularly, the invention provides a combination therapy for the treatment of a central nervous system ischemic condition or a central nervous system traumatic injury comprising the administration to a subject of a sodium ion channel blocker in combination with a cyclooxygenase-2 selective inhibitor. Use for the treatment of stroke is specifically claimed.
IT **4368-28-9**, Tetrodotoxin
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(cyclooxygenase 2 inhibitor-sodium channel blocker combination for treatment of CNS damage)
RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

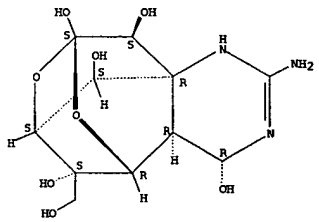
Absolute stereochemistry.

L8 ANSWER 18 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)



L8 ANSWER 19 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:757433 HCAPLUS
DOCUMENT NUMBER: 142:189796
TITLE: Advance in research of marine natural bioactive products with cardiovascular pharmacological effects
AUTHOR(S): Xu, Donghui; Wu, Zhifeng; Mei, Xueting; Xu, Shibo
CORPORATE SOURCE: Section of Drugs and Pharmacology, School of Pharmacy, Zhongshan University, Guangzhou, 510275, Peop. Rep. China
SOURCE: Zhongguo Haiyang Yaowu (2003), 22(5), 52-56
CODEN: ZHYAE8; ISSN: 1002-3461
PUBLISHER: Shandongsheng Haiyang Yaowu Kexue Yanjiuso
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Chinese
AB A review on advance in research of marine natural bioactive products with cardiovascular pharmacol. effects with subdivision headings: (1) taurine; (2) quinolone; (3) anthopleurins; (4) Anthopleura toxin; (5) Goniopora toxin; (6) tanghinoside; (7) polyunsatd. fatty acid; (8) gorgosterol; (9) tetrahydroxysterol; (10) triacetonamine; (11) tetrodotoxin and (12) Anemonia toxin, to be continued.
IT **4368-28-9**, Tetrodotoxin
RL: NPO (Natural product occurrence); PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(advance in research of marine natural bioactive products with cardiovascular pharmacol. effects)
RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

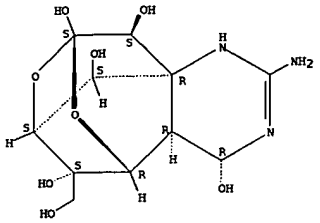
Absolute stereochemistry.



L8 ANSWER 20 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:601035 HCAPLUS
DOCUMENT NUMBER: 142:169726
TITLE: Site 1 sodium channel blockers prolong the duration of sciatic nerve blockade from tricyclic antidepressants
AUTHOR(S): Barnet, Caryn S.; Tse, Julie Y.; Kohane, Daniel S.
CORPORATE SOURCE: Department of Chemical Engineering, Massachusetts Institute of Technology, Cambridge, MA, USA
SOURCE: Pain (2004), 110(1-2), 432-438
CODEN: PAINDB; ISSN: 0304-3959
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Many recent reports in the literature address the local anesthetics efficacy of tricyclic antidepressants (TCAs). Here we investigated whether nerve block from TCAs is prolonged by site 1 sodium channel blockers such as tetrodotoxin and saxitoxin, which are known to prolong block from conventional local anesthetics. Tetrodotoxin and saxitoxin greatly prolonged block from TCAs. For example, the median duration of thermal nociceptive blocks for 10 mM amitriptyline, nortriptyline and doxepin were 0, 0, and 124 min; co-injection with 20 μM TTX (median block duration=0), yielded blocks lasting 404, 325, and 697 min, resp. Co-injection of 12 μM saxitoxin (median block duration=0) with 10 mM amitriptyline resulted in a thermal nociceptive block duration of 373 min. Co-injection of 7.7 mM bupivacaine and 7.7 mM amiptriptyline did not result in block prolongation. Systemic (s.c.) delivery of tetrodotoxin or amitriptyline did not result in prolongation of block from the other class of drug injected at the sciatic nerve. In TCA-containing formulations, motor blockade was consistently longer than thermal nociceptive block; motor blockade was also prolonged by tetrodotoxin and saxitoxin. In summary site 1 sodium channel blockers prolong the duration of TCAs via a locally mediated mechanism.
IT **4368-28-9**, Tetrodotoxin
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(site 1 sodium channel blockers tetrodotoxin combination with tricyclic antidepressants amitriptyline, nortriptyline and doxepin prolonged motor block was significantly longer than sensory block in rat)
RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L8 ANSWER 20 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)



REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 21 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:546375 HCAPLUS
DOCUMENT NUMBER: 141:99736
TITLE: method and composition comprising local anesthetics and other agents for reducing resting membrane potential elec. disturbance, and use in organ preconditioning, arrest, protection, preservation and recovery
INVENTOR(S): Dobson, Geoffrey Phillip
PATENT ASSIGNEE(S): Global Cardiac Solutions Pty Ltd, Australia
SOURCE: PCT Int. Appl., 152 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004056181	A1	20040708	WO 2003-AU1711	20031222
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
GB 2412067	A1	20050921	GB 2005-15048	20031222
US 2006034941	A1	20060216	US 2005-539222	20050617
PRIORITY APPLN. INFO.:			US 2002-436175P P	20021223
			AU 2003-900296 A	20030123
			AU 2003-903127 A	20030620
			WO 2003-AU1711 W	20031222

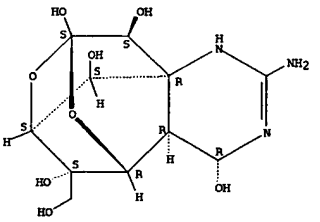
AB The invention discloses a method for reducing elec. disturbance of a cell's resting membrane potential comprising administering an effective amount of a composition comprising an effective amount of a local anesthetic and of one or more of a potassium channel opener, an adenosine receptor agonist, an anti-adrenergic, a calcium antagonist, an opioid, an NO donor and a sodium-hydrogen exchange inhibitor.

IT **4368-28-9**, Tetrodotoxin
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(local anesthetics and other agents for reducing resting membrane potential elec. disturbance, and use in organ preconditioning, arrest, protection, preservation and recovery)

RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L8 ANSWER 21 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 22 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:546374 HCAPLUS
DOCUMENT NUMBER: 141:99735
TITLE: Compositions and methods using local anesthetics and other agents for organ preconditioning, arrest, protection, preservation and recovery
INVENTOR(S): Dobson, Geoffrey Phillip
PATENT ASSIGNEE(S): Global Cardiac Solutions Pty. Ltd., Australia
SOURCE: PCT Int. Appl., 150 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004056180	A1	20040708	WO 2003-AU1710	20031222
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
PRIORITY APPLN. INFO.:			US 2002-436175P P	20021223
			AU 2003-900296 A	20030123
			AU 2003-903127 A	20030620

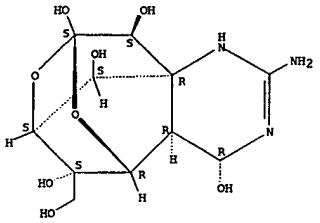
AB The invention discloses a composition for arresting, protecting or preserving a cell, tissue or organ comprising an effective amount of a local anesthetic and of one or more of an anti-adrenergic, a calcium antagonist, an opioid, an NO donor and a sodium-hydrogen exchange inhibitor.

IT **4368-28-9**, Tetrodotoxin
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(compns. and methods using local anesthetics and other agents for organ preconditioning, arrest, protection, preservation and recovery)

RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L8 ANSWER 22 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)

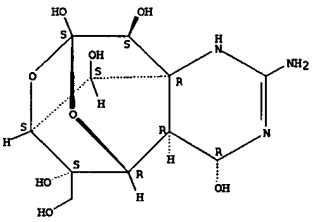


REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 23 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:514044 HCAPLUS
DOCUMENT NUMBER: 141:169243
TITLE: Cardiovascular effects of the toxin(s) of the Australian paralysis tick, Ixodes holocyclus, in the rat
AUTHOR(S): Campbell, Fiona; Atwell, Rick; Fenning, Andrew; Hoey, Andrew; Brown, Lindsay
CORPORATE SOURCE: School of Veterinary Science, The University of Queensland, Brisbane, 4072, Australia
SOURCE: Toxicon (2004), 43(7), 743-750
CODEN: TOXIA6; ISSN: 0041-0101
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB An extract of toxin(s) from the Australian paralysis tick, Ixodes holocyclus, produced pos. inotropic responses in rat left ventricular papillary muscles and pos. contractile responses in rat thoracic aortic rings. There was no measurable chronotropic response in rat right atria, but pos. inotropic concns. in papillary muscles produced arrhythmias in right atria. Pos. inotropic responses were attenuated by verapamil, but unaffected by metoprolol, cimetidine, pyrilamine, tetrodotoxin and pinacidil. Microelectrode studies on isolated left ventricular papillary muscles demonstrated that the extract prolonged action potential duration at 20, 50 and 90% of repolarization and delayed ventricular papillary muscle relaxation. Cardiovascular tissues isolated from rats with exptl. induced tick paralysis showed no myocardial damage as identified by histol. and ultrastructural examination The basal rate and force of contraction of isolated cardiac tissues were lower from tick-paralyzed than normal rats. Concentration-response curves to dobutamine and calcium chloride were similar between tissues from tick-paralyzed and normal rats. Thus, the Australian paralysis tick, I. holocyclus, produces one or more toxins with direct cardiovascular effects which mimic the effects produced by direct blockade of cardiac and vascular K+ channels.
IT **4368-28-9**, Tetrodotoxin
RL: BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(paralysis tick toxins cardiovascular effects in rat and antiarrhythmic treatment)
RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L8 ANSWER 23 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)

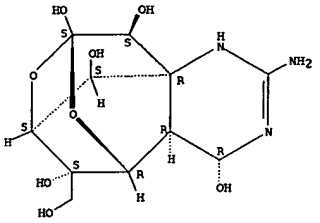


REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 24 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:486878 HCAPLUS
DOCUMENT NUMBER: 142:32376
TITLE: A novel toxicity-based assay for the identification of modulators of voltage-gated Na+ channels
AUTHOR(S): Weiser, Thomas
CORPORATE SOURCE: Boehringer Ingelheim Pharma GmbH & Co KG, Biberach, D-88397, Germany
SOURCE: Journal of Neuroscience Methods (2004), 137(1), 79-85
CODEN: JNMEDT; ISSN: 0165-0270
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Voltage-gated Na+ channels are promising drug targets. Screening of large nos. of putative modulators, however, can be demanding and expensive. In this study, a simple, cheap, and robust assay to test the pharmacol. modulation of Na+ channel function is presented. The assay makes use of the fact that the intracellular accumulation of Na+ ions can be cytotoxic. The toxicity of the Na+ channel activator veratridine in the presence of an inhibitor of the Na+/K+ATPase (ouabain) in a Nav1.2a (rat brain IIA α) expressing cell line is assessed. Na+ channel blockers should reduce toxicity in this model. CHO cells which recombinantly expressed rat Nav1.2a subunits were seeded in 96-well plates, and cell survival was tested after 24 h incubation in medium containing veratridine and ouabain in the presence or absence of Na+ channel blockers. Propidium iodide fluorescence was used as toxicity readout. Veratridine (100 μM) or ouabain alone (500 μM) were not toxic to the cells. In the presence of 500 μM ouabain, however, veratridine induced half-maximal cell death with an EC50 value of 15.1±2.3 μM. Ouabain's EC50 was 215.3±16.7 μM (with 30 μM veratridine). The effects of a number of Na+ channel blockers were tested and compared with their Na+ channel blocking activity measured in voltage-clamp expts. Blockers from various chemical classes reduced toxicity half maximally with IC50 values ranging from 11.7±1.4 nM (tetrodotoxin) to 280.5±48.0 μM (lamotrigine). There was a linear relation between the log IC50 values obtained by the two methods (slope: 1.1±0.08; correlation coefficient: 0.93). In summary, these data show that this novel toxicity assay is well suited to test Na+ channel blockers.
IT **4368-28-9**, Tetrodotoxin
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(sodium channel inhibitor tetrodotoxin reduced toxicity half maximally and suppressed cell death in chinese hamster ovary cell transfected with rat brain type Nav1.2a subunit)
RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L8 ANSWER 24 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)



REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 25 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:486383 HCAPLUS
DOCUMENT NUMBER: 141:33816
TITLE: Controlled-release pharmaceuticals for prolonged suppression of electrical activity in excitable tissues, and use in the treatment of epilepsy and other conditions
INVENTOR(S): Kohane, Daniel S.; Langer, Robert S.
PATENT ASSIGNEE(S): Massachusetts Institute of Technology, USA; The General Hospital Corporation
SOURCE: PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004050034	A2	20040617	WO 2003-US38406	20031202
WO 2004050034	A3	20050428		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2005202093	A1	20050915	US 2003-727032	20031202

PRIORITY APPLN. INFO.: US 2002-430240P P 20021202

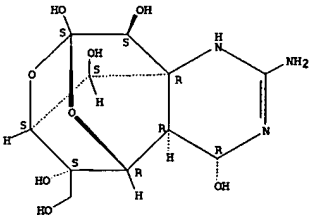
AB Controlled release of pharmaceutical agents using microspheres or other controlled release systems are used to treat disease state characterized by aberrant elec. activity in excitable tissue. For the treatment of epilepsy, agents useful in the treatment of epilepsy may be delivered to the patient at the site of seizure origin to control seizure activity in a time release manner. The system may also be useful in the treatment of cardiac arrhythmias and preterm labor. Particularly useful pharmaceutical compns. comprising a site 1 sodium channel blocker are also provided.

IT **4368-28-9**, Tetrodotoxin
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(controlled-release pharmaceuticals for prolonged suppression of elec. activity in excitable tissues, and use in treatment of epilepsy and other conditions)

RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L8 ANSWER 25 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)



L8 ANSWER 26 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:475248 HCAPLUS
DOCUMENT NUMBER: 141:238048
TITLE: Prolonged infusion of tetrodotoxin does not block mossy fiber sprouting in pilocarpine-treated rats
AUTHOR(S): Buckmaster, Paul S.
CORPORATE SOURCE: Departments of Comparative Medicine and Neurology & Neurological Sciences, Stanford University, Palo Alto, CA, USA
SOURCE: Epilepsia (2004), 45(5), 452-458
CODEN: EPILAK; ISSN: 0013-9580
PUBLISHER: Blackwell Publishing, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

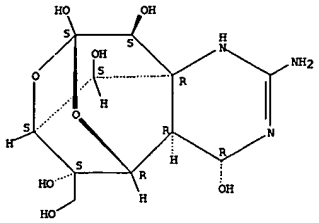
AB Mossy fiber sprouting is a common abnormality found in patients and models of temporal lobe epilepsy. The role of mossy fiber sprouting in epileptogenesis is unclear, and its blockade would be useful exptl. and perhaps therapeutically. Results from previous attempts to block mossy fiber sprouting have been disappointing or controversial. In some brain regions, prolonged application of the sodium channel blocker tetrodotoxin prevents axon sprouting and posttrauma epileptogenesis. The present study tested the hypothesis that prolonged, focal infusion of tetrodotoxin would block mossy fiber sprouting after an epileptogenic treatment. Adult rats were treated with pilocarpine to induce status epilepticus. Several hours to 3 days after pilocarpine treatment, a pump with a cannula directed toward the dentate gyrus was implanted to deliver 10 μM tetrodotoxin or vehicle alone at 0.25 μl/h. This method blocks local EEG activity in the hippocampus (Galvan et al. J Neurosci 2000; 20:2904-16). After 28 days of continuous infusion, rats were perfused with fixative, and their hippocampi analyzed anatomically with stereol. techniques. Tetrodotoxin infusion was verified immunocytochem. in tetrodotoxin-treated but not vehicle-treated hippocampi. Tetrodotoxin-infused and vehicle-infused hippocampi displayed similar levels of hilar neuron loss. The Timm stain revealed mossy fiber sprouting regardless of whether hippocampi were treated with tetrodotoxin infusion, vehicle infusion, or neither. Prolonged infusion of tetrodotoxin did not block mossy fiber sprouting. This finding suggests that sodium channel-mediated neuronal activity is not necessary for mossy fiber sprouting after an epileptogenic treatment.

IT **4368-28-9**, Tetrodotoxin
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(tetrodotoxin prolonged infusion does not block mossy fiber sprouting in pilocarpine-treated rats)

RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L8 ANSWER 26 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)



REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 27 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:284577 HCAPLUS
DOCUMENT NUMBER: 140:368272
TITLE: Particular sensitivity to calcium channel blockers of the fast inward voltage-dependent sodium current involved in the invasive properties of a metastatic breast cancer cell line
AUTHOR(S): Roger, Sebastien; Le Guennec, Jean-Yves; Besson, Pierre
CORPORATE SOURCE: Nutrition, Croissance et Cancer, Emi-U 0211, Faculte de Medecine, Tours, 37032, Fr.
SOURCE: British Journal of Pharmacology (2004), 141(4), 610-615
CODEN: BJPCBM; ISSN: 0007-1188
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English

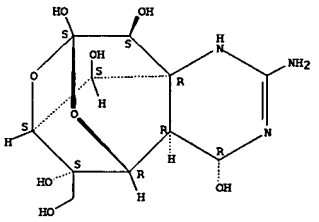
AB A voltage-dependent sodium current has been described in the highly invasive breast cancer cell line MDA-MB-231. Its activity is associated with the invasive properties of the cells. The aim of our study was to test whether this current (INa) is sensitive to three representative calcium channel blockers: verapamil, diltiazem and nifedipine. INa was studied in patch-clamp conditions. INa was sensitive to verapamil (IC50 = 37.6±2.5 μM) and diltiazem (53.2±3.6 μM), while it was weakly sensitive to nifedipine. The tetrodotoxin (TTX) concentration, which fully blocks INa (30 μM), did not affect cell proliferation. Diltiazem and verapamil, at concns. that do not fully block INa, strongly reduced cell proliferation, suggesting, regarding proliferation, that these mols. act on targets distinct from sodium channels. These targets are probably not other ionic channels, since the current measured at the end of a 500 ms long pulse in the voltage range between -60 and +40 mV was unaffected by verapamil and diltiazem. We conclude that the sodium channel expressed in MDA-MB-231 cells is sensitive to several calcium channel blockers. The present study also underlines the danger of concluding the possible involvement of membrane channel proteins in any phenomenon on the sole basis of pharmacol., and without an electrophysiol. confirmation.

IT **4368-28-9**, Tetrodotoxin
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(sensitivity to calcium channel blockers of fast inward voltage-dependent sodium current characteristic of metastatic breast cancer cells)

RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

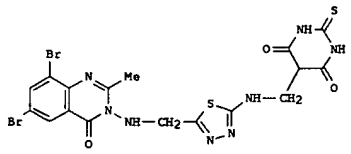
L8 ANSWER 27 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)



REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 28 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:151294 HCAPLUS
DOCUMENT NUMBER: 140:368075
TITLE: Synthesis of some newer derivatives of substituted quinazolinonyl-2-oxo/thiobarbituric acid as potent anticonvulsant agents
AUTHOR(S): Archana; Srivastava, V. K.; Kumar, Ashok
CORPORATE SOURCE: Department of Pharmacology, Medicinal Chemistry Division, L.L.R.M. Medical College, Meerut (U.P.), 250004, India
SOURCE: Bioorganic & Medicinal Chemistry (2004), 12(5), 1257-1264
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 140:368075
GI



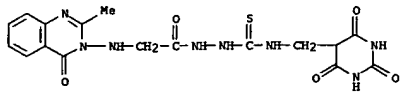
I

AB 5-{1'-[3''-Aminoacetyl-2''-methyl-6'',8''-dihalosubstitutedquinazolin-4''(3''H)-onyl]-thiosemicarbazido)-2-oxo/thiobarbituric acids and 5-{2'-amino-5'-[3''-aminomethylene-2''-methyl-6'',8''-dihalosubstitutedquinazolin-4''(3''H)-onyl]-1',3',4'-thiadiazol-2'-yl}-2-oxo/thiobarbituric acid were prepared by incorporating 1-[3'-aminoacetyl-2'-methyl-6'',8''-dihalosubstituted-quinazolin-4'(3'H)-onyl]-thiosemicarbazides and 2-amino-5-[3'-aminomethylene-2'-methyl-6',8'-dihalosubstituted-quinazolin-4'(3'H)-onyl]-1,3,4-thiadiazoles resp. at 5th position of 2-oxo/thiobarbituric acids (via Mannich reaction). All the newly synthesized compds. were screened for their anti-convulsant activity in MES and PTZ models and were compared with standard drugs phenytoin sodium and sodium valproate. Interestingly, these compds. were found to be devoid of sedative and hypnotic activities when tested. Out of the compds. studied, the most active compound I showed activity (90%) more potent than the standard drug.

IT **683236-24-0P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis of quinazolinonyl-2-oxo/thiobarbituric acids as potent anticonvulsant agents)

RN 683236-24-0 HCAPLUS
CN Glycine, N-(2-methyl-4-oxo-3(4H)-quinazolinyl)-, 2-[[[(hexahydro-2,4,6-trioxo-5-pyrimidinyl)methyl]amino]thioxomethyl]hydrazide (9CI) (CA INDEX NAME)

L8 ANSWER 28 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)



REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 29 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:80526 HCAPLUS
DOCUMENT NUMBER: 140:144688
TITLE: Hapten-carrier conjugates comprising hormone, toxin, or drug for diagnosis and therapy
INVENTOR(S): Bachmann, Martin F.; Maurer, Patrik
PATENT ASSIGNEE(S): Cytos Biotechnology Ag, Switz.
SOURCE: PCT Int. Appl., 144 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004009116	A2	20040129	WO 2003-EP7850	20030718
WO 2004009116	A3	20040318		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2487849	AA	20040129	CA 2003-2487849	20030718
AU 2003250106	A1	20040209	AU 2003-250106	20030718
US 2004059094	A1	20040325	US 2003-622064	20030718
US 6932971	B2	20050823		
BR 2003012297	A	20050412	BR 2003-12297	20030718
EP 1523334	A2	20050420	EP 2003-765047	20030718
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2006504654	T2	20060209	JP 2004-522508	20030718
US 2005281845	A1	20051222	US 2005-125402	20050510

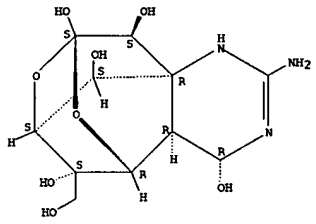
PRIORITY APPLN. INFO.:			
US 2002-396575P	P	20020718	
US 2003-622064	A3	20030718	
WO 2003-EP7850	W	20030718	

AB The present invention provides compns. comprising a conjugate of a hapten with a carrier in an ordered and repetitive array, and methods of making such compns. The conjugates and compns. of the invention may comprise a variety of haptens, including hormones, toxins and drugs, especially drugs of addiction such as nicotine. Compns. and conjugates of the invention are useful for inducing immune responses against haptens, which can use useful in a variety of therapeutic, prophylactic and diagnostic regimens. In certain embodiments, immune responses generated using the conjugates, compns. and methods of the present invention are useful to prevent or treat addiction to drugs of abuse and the resultant diseases associated with drug addiction.

IT **4368-28-9P**, Tetrodotoxin
RL: ARU (Analytical role, unclassified); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); **THU (Therapeutic use)**; ANST (Analytical study); BIOL (Biological study);

L8 ANSWER 29 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)
PREP (Preparation); USES (Uses)
(conjugates; hapten-carrier conjugates comprising a hormone, toxin, or drug and a core particle of bacteriophage protein for diagnosis and therapy)
RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L8 ANSWER 30 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:80465 HCAPLUS
DOCUMENT NUMBER: 140:139471
TITLE: Preparation of of quinazolinone-like derivatives to treat cellular proliferative diseases
INVENTOR(S): Bergnes, Gustave; Smith, Whitney W.; Yao, Bing; Morgans, David J., Jr.; MacDonald, Andrew
PATENT ASSIGNEE(S): Cytokinetics, Inc., USA
SOURCE: PCT Int. Appl., 64 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004009036	A2	20040129	WO 2003-US23319	20030723
WO 2004009036	A3	20040819		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004142949	A1	20040722	US 2003-626012	20030723
EP 1537089	A2	20050608	EP 2003-766028	20030723
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2006501201	T2	20060112	JP 2004-523405	20030723

PRIORITY APPLN. INFO.:			
US 2002-398224P	P	20020723	
WO 2003-US23319	W	20030723	

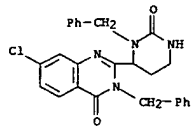
OTHER SOURCE(S): MARPAT 140:139471

AB The invention relates to quinazolinone-like derivs. that are inhibitors of the mitotic kinesin KSP and are useful in the treatment of cellular proliferative diseases, for example cancer, hyperplasias, restenosis, cardiac hypertrophy, immune disorders and inflammation. Preparation of 3-Benzyl-7-chloro-2-(3-benzyl-2-oxohexahydropyrimidin-4-yl)-3H-quinazolin-4-one is included.

IT **651323-36-3P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of quinazolinone derivs. to treat cellular proliferative diseases)
RN 651323-36-3 HCAPLUS
CN 4(3H)-Quinazolinone, 7-chloro-2-[hexahydro-2-oxo-3-(phenylmethyl)-4-pyrimidinyl]-3-(phenylmethyl)- (9CI) (CA INDEX NAME)

Prepare Publication

L8 ANSWER 30 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)



L8 ANSWER 31 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:62959 HCAPLUS
DOCUMENT NUMBER: 141:155568
TITLE: An experimental vaccine against tetrodotoxin with longer term of validity
AUTHOR(S): Xu, Qinhui; Wei, Changhua; Huang, Kai; Gao, Lisha; Rong, Kangtai; Yun, Liuhong
CORPORATE SOURCE: Institute of Pharmacology and Toxicology, Academy of Military Medical Sciences, Beijing, 100850, Peop. Rep. China
SOURCE: Zhongguo Mianyixue Zazhi (2003), 19(5), 339-342
CODEN: ZMZAEE; ISSN: 1000-484X
PUBLISHER: Zhongguo Mianyixue Zazhi Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

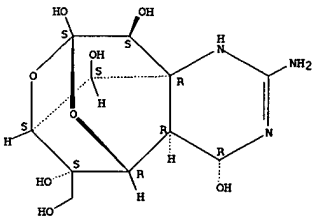
AB Objective: To develop an antitoxin vaccine against tetrodotoxin (TTX) and to explore the possibility of immune prevention and treatment for TTX intoxication. Methods: TTX was conjugated with Tachypleus tridentatus hemocyanin (TTH) in presence of formaldehyde and applied to immunize Balb/C mice. The level of antisera in the animals was periodically measured by ELISA and competition-inhibited enzyme immunoassay (CIEIA). Mice immunized with TTX-TTH were challenged i.p. with low doses of TTX (1LD= 13.5 μg/kg). Results: The high titer and affinity of antisera lasted for as long as more than one year. The immunized mice were i.p. challenged with 1xLD of TTX once and again at a fixed period, there was a affirmative antitoxic effect in about 12 mo (total 15xLD), and a partial effect in following time. About one fourth of animal survived till 24 mo post initial immunization (total 26xLD), and which was a stage of senescence in mice. The anti-TTX poisoning effect of animal was consistent with the antisera quality tested. Conclusions: The exptl. vaccine of TTX could effectively protect animal from TTX intoxication and its effect was of longer duration of validity. Immunoprophylaxis would be the hopeful means for detoxification of TTX.

IT **4368-28-9**, Tetrodotoxin
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(Tachypleus tridentatus hemocyanin conjugates; tetrodotoxin vaccine with longer term of validity)

RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L8 ANSWER 31 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)



L8 ANSWER 32 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:60544 HCAPLUS
DOCUMENT NUMBER: 140:144682
TITLE: Molecular antigen arrays comprising AP205 virus-like particle and antigen for prevention and treatment of cancer, drug addiction, poisoning, infection, and allergy
INVENTOR(S): Bachmann, Martin F.; Tissot, Alain; Pumpens, Paul; Cielens, Indulis; Renhofa, Regina
PATENT ASSIGNEE(S): Cytos Biotechnology AG, Switz.
SOURCE: PCT Int. Appl., 170 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

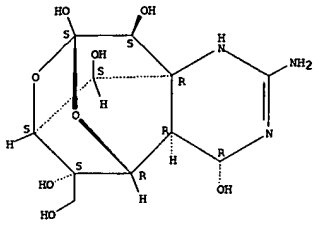
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004007538	A2	20040122	WO 2003-EP7572	20030714
WO 2004007538	A3	20040304		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2489410	AA	20040122	CA 2003-2489410	20030714
AU 2003246690	A1	20040202	AU 2003-246690	20030714
US 2004076611	A1	20040422	US 2003-617876	20030714
EP 1532167	A2	20050525	EP 2003-763829	20030714
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003012935	A	20050621	BR 2003-12935	20030714
PRIORITY APPLN. INFO.:			US 2002-396126P	P 20020717
			WO 2003-EP7572	W 20030714

AB The present invention provides a composition comprising an AP205 virus like particle (VLP) and an antigen. The invention also provides a process for producing an antigen or antigenic determinant bound to AP205 VLP. AP205 VLP bound to an antigen is useful in the production of compns. for inducing immune responses that are useful for the prevention or treatment of diseases, disorders or conditions including infectious diseases, allergies, cancer, drug addiction, poisoning and to efficiently induce self-specific immune responses, in particular antibody responses.

IT **4368-28-9P**, Tetrodotoxin
RL: ARU (Analytical role, unclassified); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); **THU (Therapeutic use)**; ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(mol. antigen arrays comprising AP205 virus-like particle and antigen for prevention and treatment of cancer, drug addiction, poisoning, infection, and allergy)

RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

L8 ANSWER 32 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)
Absolute stereochemistry.



L8 ANSWER 33 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:41272 HCAPLUS
DOCUMENT NUMBER: 140:99642
TITLE: Novel medicament combinations based on sodium channel blockers and magnesium salts
INVENTOR(S): Duettmann, Hermann; Weiser, Thomas
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma G.m.b.H. & Co. K.-G., Germany
SOURCE: PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

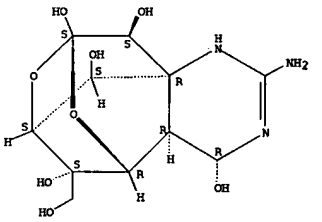
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004004723	A1	20040115	WO 2003-EP6665	20030625
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10230027	A1	20040122	DE 2002-10230027	20020704
CA 2491217	AA	20040115	CA 2003-2491217	20030625
AU 2003246582	A1	20040123	AU 2003-246582	20030625
EP 1521579	A1	20050413	EP 2003-762507	20030625
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2005532376	T2	20051027	JP 2004-518563	20030625
US 2004087513	A1	20040506	US 2003-612107	20030702

PRIORITY APPLN. INFO.:			
	DE 2002-10230027	A	20020704
	US 2002-408213P	P	20020904
	WO 2003-EP6665	W	20030625

OTHER SOURCE(S): MARPAT 140:99642
AB The invention relates to novel medicament combinations based on sodium channel blockers and magnesium salts. The invention also relates to a method for the production thereof and the use thereof in the production of medicaments for the treatment of ischemic states. The sodium channel blockers and magnesium salts are administered parenteral; magnesium salts can be administered orally. The two components can be included in sep. formulations or in one formulation. Thus a sodium channel blocker injection contained (mg): crobenetine hydrochloride 767; hydroxypropyl γ-cyclodextrin 10000; mannitol 11000; acetic acid (99%) 125.25; sodium acetate trihydrate 56.5; and water to 250 mL. A magnesium salt injection contained 1000 mg magnesium sulfate and 10 mL water..
IT **4368-28-9**, Tetrodotoxin
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(medicament combinations based on sodium channel blockers and magnesium salts)
RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-

L8 ANSWER 33 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)
pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 34 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:20436 HCAPLUS
DOCUMENT NUMBER: 140:92564
TITLE: Use of mixtures of related antigenic peptides to induce a cytotoxic T lymphocyte immune response in a wide range of individuals
INVENTOR(S): Ruprecht, Ruth M.; Jiang, Shisong
PATENT ASSIGNEE(S): Dana-Farber Cancer Institute, Inc., USA
SOURCE: PCT Int. Appl., 175 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

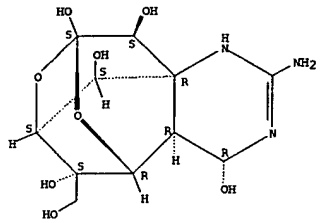
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004002415	A2	20040108	WO 2003-US20322	20030627
WO 2004002415	C2	20040603		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2005249742	A1	20051110	US 2004-22562	20041222

PRIORITY APPLN. INFO.:			
	US 2002-392718P	P	20020627
	WO 2003-US20322	A1	20030627

AB The present invention provides compns. and methods for the treatment and prevention of immune disorders. A method of inducing an effective cytotoxic T lymphocyte (CTL) immune response in a wide range of individuals using mixts. of related antigenic pep ides (Overlapping Synthetic Peptide Formulations (OSPFs)) is described. OSPFs are derived from a longer antigenic peptide by splitting it up into peptides of at least eight amino acids with an overlap of at least one C-terminal amino acid from one peptide with the N-terminus of the next fragment. Use of an overlapping peptide library of the gag protein of HIV-1 to induce CTL responses in BALB/c and C57BL/6 mice is demonstrated. They also induced a proliferative T helper cell response.
IT **4368-28-9**, Tetrodotoxin
RL: ADV (Adverse effect, including toxicity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(vaccines against, overlapping synthetic peptide formulations for; use of mixts. of related antigenic peptides to induce cytotoxic T lymphocyte immune response in wide range of individuals)
RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L8 ANSWER 34 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)



L8 ANSWER 35 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:1006769 HCAPLUS
DOCUMENT NUMBER: 140:47530
TITLE: Medicament combinations of sodium channel blockers and fibrinolytics for treating ischemic conditions
INVENTOR(S): Banzet, Sophie; Duettmann, Hermann; Mauz, Annerose
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma G.m.b.H. & Co. K.-G., Germany
SOURCE: PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003105844	A1	20031224	WO 2003-EP5813	20030604
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10226814	A1	20040108	DE 2002-10226814	20020615
CA 2485751	AA	20031224	CA 2003-2485751	20030604
AU 2003250338	A1	20031231	AU 2003-250338	20030604
EP 1515720	A1	20050323	EP 2003-759907	20030604
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2005536478	T2	20051202	JP 2004-512748	20030604
US 2003235576	A1	20031225	US 2003-460709	20030612

PRIORITY APPLN. INFO.:
DE 2002-10226814 A 20020615
US 2002-408144P P 20020904
WO 2003-EP5813 W 20030604

OTHER SOURCE(S): MARPAT 140:47530

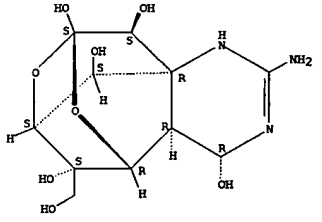
AB The invention relates to novel medicament combinations based on sodium channel blockers and fibrinolytics, to a method for producing the same and to the use thereof for producing medicaments for treating ischemic conditions. The selected sodium channel blockers and fibrinolytics can be prepared as one formulation or as two formulations. The synthesis of benzazocine compds. that are sodium channel blockers is described. An injection formulation containing the sodium channel blocker included: crobenetine hydrochloride 767 mg; hydroxypropyl γ-cyclodextrin 10000 mg; mannitol 11000 mg; acetic acid (99%) 125.25; sodium acetate trihydrate 56.6; water to 250 mL.

IT **4368-28-9**, Tetrodotoxin
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(medicament combinations of sodium channel blockers and fibrinolytics for treating ischemic conditions)

RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-,

L8 ANSWER 35 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)
(4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 36 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN

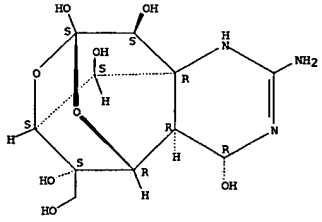
ACCESSION NUMBER: 2003:996337 HCAPLUS
DOCUMENT NUMBER: 141:976
TITLE: Analgesic effects of TTX alone and combined with morphine on formalin test in rats
AUTHOR(S): Xu, Ying; Geng, Xingchao; Han, Jisheng; Qi, Shiquan; Ku, Baoshai
CORPORATE SOURCE: Department of Pharmacology, school of Basic Medical Sciences, Peking University, Beijing, 100083, Peop. Rep. China
SOURCE: Zhongguo Haiyang Yaowu (2003), 22(2), 39-41, 56
CODEN: ZHYAE8; ISSN: 1002-3461
PUBLISHER: Shandongsheng Haiyang Yaowu Kexue Yanjiuso
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

AB The effects of tetrodotoxin (TTX) alone and combined with morphine on formalin-induced pain model were studied in rats. TTX, morphine, or both were administered i.m. and their effects were measured. Data were expressed as the median ID (ID50). The ID50 of TTX alone was 0.8 μg kg-1. The ID50 of Morphine alone was 2.6 mg kg-1. The combination of TTX (39 μg kg-1 or 0.19 μg kg- 1) and morphine showed more potent than each of them alone. The ID50 of Morphine reduced to 0.5 mg kg-1 and 1.1 mg kg-1, resp. An isobologram showed synergistic effect between TTX and morphine. The results indicated that TTX had analgesic effect in the formalin-induced pain model in rats. Comparing the effects of TTX alone and combined with morphine, the latter revealed a synergistic effect.

IT **4368-28-9**, Tetrodotoxin
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(analgesic effects of TTX alone and combined with morphine on formalin test in rats)

RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



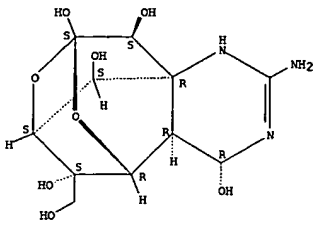
L8 ANSWER 37 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:841693 HCAPLUS
DOCUMENT NUMBER: 141:135585
TITLE: Purification of tetrodotoxin with cationic exchange and gel filtration chromatograph for pharmaceutical and analytical use
INVENTOR(S): Jin, Chuanyin; Liu, Yongding; Song, Lirong; Zhu, Jiaming
PATENT ASSIGNEE(S): Institute of Aquatic Biology, Chinese Academy of Sciences, Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 6 pp. CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1385432	A	20021218	CN 2001-114201	20010515
PRIORITY APPLN. INFO.:			CN 2001-114201	20010515

AB Method of the invention comprises adsorbing tetrodotoxin on the NH4+- or H+-type weakly cationic exchange resin column, washing with water (buffer, or <0.4N acetic acid solution), eluting with 0.1- 0.2N acetic acid as eluent or 0.01-2.5N acetic acid as gradient eluent, concentrating, dissolving in 0.01-0.15N acetic acid (or picric acid); purifying on gel filtration column with 0.01-0.15N acetic acid as eluent, and concentrating to obtain tetrodotoxin acetate (or tetrodotoxin picrate). The tetrodotoxin picrate may be converted into tetrodotoxin acetate by dissolving in water, precipitating in NH4OH at pH 9, and dissolving in acetic acid.
IT **4368-28-9P**, Tetrodotoxin
RL: ARU (Analytical role, unclassified); BUU (Biological use, unclassified); PUR (Purification or recovery); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(purification of tetrodotoxin with cationic exchange and gel filtration chromatograph for pharmaceutical and anal. use)
RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L8 ANSWER 37 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)

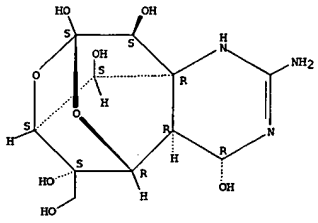


L8 ANSWER 38 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:519407 HCAPLUS
DOCUMENT NUMBER: 140:169452
TITLE: Prolonged duration local anesthesia from tetrodotoxin-enhanced local anesthetic microspheres
AUTHOR(S): Kohane, Daniel S.; Smith, Sarah E.; Louis, David N.; Colombo, Gaia; Ghoroghchian, Peter; Hunfeld, Nicole G. M.; Berde, Charles B.; Langer, Robert
CORPORATE SOURCE: Massachusetts Institute of Technology and Department of Anesthesia, and Research Associate, Massachusetts General Hospital and Harvard Medical School, Children's Hospital, Boston, MA, USA
SOURCE: Pain (2003), 104(1,2), 415-421 CODEN: PAINDB; ISSN: 0304-3959
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB There is interest in developing prolonged duration local anesthetics. Here the authors examine whether tetrodotoxin (TTX) can be used to prolong the block from bupivacaine microspheres with and without dexamethasone. Rats received sciatic nerve blocks with 75 mg of microspheres containing 0.05% (weight/weight) TTX, 50% (weight/weight) bupivacaine and/or 0.05% (weight/weight) dexamethasone. 0.1% (weight/weight) TTX microspheres were also tested. The carrier fluid contained 1:100,000 epinephrine. Nociceptive and motor blockade of the hindpaw were quantified. Nerves and adjacent muscles were harvested 2 wk after injection for histol. assessment by light microscopy. The median nociceptive block duration in hours from the microsphere groups were: bupivacaine = 6.2, 0.05% TTX = 0, bupivacaine + TTX = 35.3, bupivacaine + dexamethasone = 31.3, TTX + dexamethasone = 8.1, TTX + bupivacaine + dexamethasone = 221.7. Some animals receiving particles containing 0.05% TTX had deficits in the uninjected extremity; all animals receiving 0.1% (weight/weight) TTX particles died. Pockets of particles were associated with localized inflammation, and all samples showed some evidence of myotoxicity in the vicinity of the injection. The nerves themselves appeared intact. In summary, coencapsulation of TTX in controlled release devices containing bupivacaine and dexamethasone resulted in very prolonged nerve blocks. As formulated here, this preparation had a narrow margin of safety. While the myotoxicity appears consistent with the well-known reversible myotoxicity associated with local anesthetics, its long-term significance remains to be established.
IT **4368-28-9**, Tetrodotoxin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prolonged duration local anesthesia from tetrodotoxin-enhanced local anesthetic microspheres)
RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L8 ANSWER 38 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)



REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

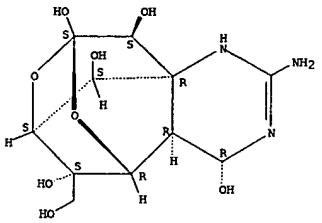
L8 ANSWER 39 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:319348 HCAPLUS
DOCUMENT NUMBER: 138:331688
TITLE: Methods of suppressing microglial activation and systemic inflammatory responses
INVENTOR(S): Laskowitz, Daniel T.; Matthew, William D.; McMillian, Michael
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 48 pp., Cont.-in-part of U.S. Ser. No. 957,909.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003077641	A1	20030424	US 2002-252120	20020923
US 2002164789	A1	20021107	US 2001-957909	20010921
PRIORITY APPLN. INFO.:			US 1998-77551P	P 19980311
			US 1999-260430	B2 19990301
			US 2001-957909	A2 20010921

AB Methods of suppressing the activation of microglial cells in the Central Nervous System (CNS), methods of ameliorating or treating the neurol. effects of cerebral ischemia or cerebral inflammation, and methods of combating specific diseases that affect the CNS by administering a compound that binds to microglial receptors and prevents or reduces microglial activation are described. ApoE receptor binding peptides that may be used in the methods of the invention are also described, as are methods of using such peptides to treat peripheral inflammatory conditions such as sepsis. Also described are methods of screening compds. for the ability to suppress or reduce microglial activation. Injection of ApoE (133-149) in mice suppressed serum levels of TNFα and IL-6 following LPS administration.
IT 4368-28-9, Tetrodotoxin
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anticonvulsant; ApoE receptor binding peptides suppressing microglial activation and systemic inflammatory responses)
RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L8 ANSWER 39 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)

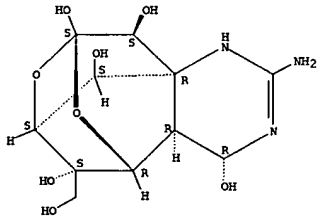


L8 ANSWER 40 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:196097 HCAPLUS
DOCUMENT NUMBER: 139:317174
TITLE: DOPA cyclohexyl ester potently inhibits aglycemia-induced release of glutamate in rat striatal slices
AUTHOR(S): Hashimoto, Mizuki; Miyamae, Takeaki; Yamamoto, Isao; Goshima, Yoshio
CORPORATE SOURCE: Department of Molecular Pharmacology and Neurobiology, Yokohama City University School of Medicine, Yokohama, 236-0004, Japan
SOURCE: Neuroscience Research (Oxford, United Kingdom) (2003), 45(3), 335-344
CODEN: NERADN; ISSN: 0168-0102
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Brain ischemic insult causes glutamate release and resultant neuronal cell death. We here show that L-3,4-dihydroxyphenylalanine (DOPA) is a pos. regulatory factor for glutamate release elicited by a mild brain insult using in vitro superfused rat striatal slices as a model system. Glucose deprivation for 18 min elicited release of glutamate, DOPA and dopamine (DA). Either tetrodotoxin (TTX) (1 μM) or α-methyl-p-tyrosine (α-MPT) (1 mM), a tyrosine hydroxylase inhibitor reduced markedly each of these releases. NSD-1015 (20 μM), an aromatic l-amino acid decarboxylase inhibitor restored the inhibition by α-MPT of glutamate and DOPA but not DA release. DOPA cyclohexyl ester (DOPA CHE) (0.3-1 μM), a competitive DOPA antagonist, concentration-dependently suppressed aglycemia-induced glutamate release, the effect which was mimicked neither by S-sulpiride nor SCH23390, a DA D1 or D2 receptor antagonist, resp. Zonisamide (1-1000 μM), an anticonvulsant or YM872 (1 μM), an α-amino-3-hydroxy-5-methyl-4-isoxazole propionic acid (AMPA) a receptor antagonist produced no effect on aglycemia-induced glutamate release. DOPA CHE thus showed a relatively potent inhibitory action on aglycemia-induced glutamate release among several neuroprotective agents tested.
IT 4368-28-9, Tetrodotoxin
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(DOPA cyclohexyl ester potently inhibits aglycemia-induced release of glutamate in rat striatum)
RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L8 ANSWER 40 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)



REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 41 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:76880 HCAPLUS
DOCUMENT NUMBER: 138:119602
TITLE: Methods of generating human cardiac cells and tissues and uses thereof
INVENTOR(S): Gepstein, Lior; Kehat, Izhak; Itskovitz-eldor, Joseph; Amit, Michal
PATENT ASSIGNEE(S): Technion Research and Development Foundation Ltd., Israel
SOURCE: PCT Int. Appl., 147 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003008535	A2	20030130	WO 2002-IL606	20020721
WO 2003008535	A3	20031023		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2005037489	A1	20050217	US 2004-759734	20040120
PRIORITY APPLN. INFO.:			US 2001-306462P P	20010720
			WO 2002-IL606 A2	20020721

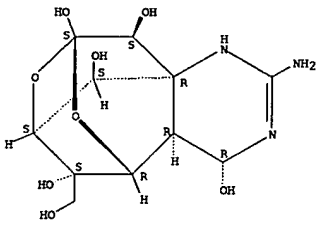
AB A method of generating cells predominantly displaying at least one characteristic associated with a cardiac phenotype is disclosed. The method comprises (a) partially dispersing a confluent cultured population of human stem cells, thereby generating a cell population including cell aggregates; (b) subjecting said cell aggregates to culturing conditions suitable for generating embryoid bodies; (c) subjecting said embryoid bodies to culturing conditions suitable for inducing cardiac lineage differentiation in at least a portion of the cells of said embryoid bodies, said culturing conditions suitable for inducing cardiac lineage differentiation including adherence of said embryoid bodies to a surface, and culture medium supplemented with serum, thereby generating cells predominantly displaying at least one characteristic associated with a cardiac phenotype.

IT **4368-28-9**, Tetrodotoxin
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(methods of generating human cardiac cells and tissues and uses thereof)

RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L8 ANSWER 41 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)



L8 ANSWER 42 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:5786 HCAPLUS
DOCUMENT NUMBER: 138:49952
TITLE: Use of sodium channel blockers and aspirin in manufacturing drugs for producing analgesia synergistically in mammals
INVENTOR(S): Xu, Baoshan; Shum, Hay Kong
PATENT ASSIGNEE(S): Wex Medical Instrumentation Co., Ltd., Peop. Rep. China
SOURCE: PCT Int. Appl., 11 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003000268	A1	20030103	WO 2002-CN428	20020618
WO 2003000268	C1	20040304		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CN 1393223	A	20030129	CN 2001-115990	20010622
CA 2493885	AA	20030103	CA 2002-2493885	20020618
EP 1405639	A1	20040407	EP 2002-754135	20020618
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004534821	T2	20041118	JP 2003-506913	20020618
US 2004192659	A1	20040930	US 2004-480288	20040401
PRIORITY APPLN. INFO.:			CN 2001-115990 A	20010622
			WO 2002-CN428 W	20020618

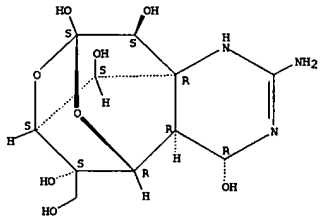
AB The present invention relates to the use of combinations of sodium channel blocking compds. and aspirin in manufacturing drugs for producing synergistically analgesic effect in mammals, in which said compds. bind to α-subunit of SS1 or SS2 sites in the sodium channel. According to the invention, pharmaceutical compns. have enhancing analgesic effect, and therefore dosage of aspirin as well as its side effects would be reduced.

IT **4368-28-9**, TTX
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(use of sodium channel blockers and aspirin in manufacturing drugs for producing analgesia synergistically in mammals)

RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L8 ANSWER 42 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)



L8 ANSWER 43 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:905867 HCAPLUS
DOCUMENT NUMBER: 137:363099
TITLE: Analgesic composition and method
INVENTOR(S): Ku, Baoshan; Shum, Frank Hay Kong
PATENT ASSIGNEE(S): Wex Medical Instrumentation Co., Ltd., Peop. Rep. China
SOURCE: PCT Int. Appl., 35 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002094272	A1	20021128	WO 2002-CN339	20020520
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CN 1386505	A	20021225	CN 2001-118098	20010518
US 2002198226	A1	20021226	US 2002-62483	20020205
US 6780866	B2	20040824		
CA 2485337	AA	20021128	CA 2002-2485337	20020520
EP 1387685	A1	20040211	EP 2002-734980	20020520
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004529959	T2	20040930	JP 2002-590989	20020520
US 2004214842	A1	20041028	US 2004-849240	20040520

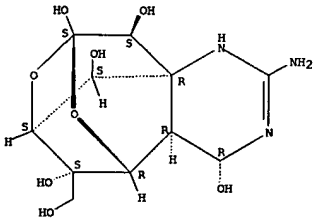
PRIORITY APPLN. INFO.: CN 2001-118098 A 20010518
US 2002-62483 A3 20020205
WO 2002-CN339 W 20020520

AB A pharmaceutical analgesic composition comprising an opioid analgesic agent and a compound that binds to the SS1 or SS2 subunit of a sodium channel, such as tetrodotoxin and saxitoxin, and analogs thereof. Administration of an opioid analgesic agent and a compound that binds to the SS1 or SS2 subunit of a sodium channel, such as tetrodotoxin and saxitoxin, and their analogs, produces analgesia in the treatment of pain in mammals. For example, the synergistic analgesia effect produced by co-administering tetrodotoxin (TTX) and morphine was observed in a formalin test in rats. Morphine used alone at 0.30 mg/kg only produced 10.2% inhibition of formalin-induced pain. Combination of TTX at 0.19 μg/kg with morphine at 2.50 mg/kg increased the inhibition rate to 86.7% from 34.9% where the latter was used alone. TTX at a dose of 0.39 μg/kg (1/50 of LD50) produced an inhibition rate of 32.9% when used alone and 66.2% in combination with 0.15 mg/kg of morphine, whereas the latter only produced an inhibition rate of 7.2% when used alone.

IT **4368-28-9**, Tetrodotoxin
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)

L8 ANSWER 43 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)
(synergistic analgesic activity of combination of opioid and sodium channel blocker)
RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 44 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:833513 HCAPLUS
DOCUMENT NUMBER: 137:304801
TITLE: Method of local anesthesia and analgesia using sodium channel blockers and local anesthetics
INVENTOR(S): Liu, Yuling; Yin, Wenjuan
PATENT ASSIGNEE(S): Wex Medical Instrumentation Co., Ltd., Hong Kong
SOURCE: U.S. Pat. Appl. Publ., 7 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

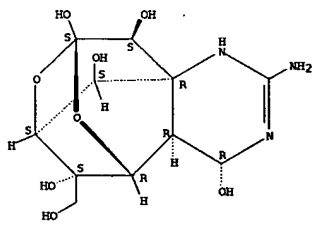
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002161013	A1	20021031	US 2001-6122	20011210
CN 1382443	A	20021204	CN 2001-110498	20010425

PRIORITY APPLN. INFO.: CN 2001-110498 A 20010426

AB The invention relates to a method of obtaining local anesthesia and analgesia to the nerve tissue region of a mammal by administration of an ED of sodium channel blocking compds., including tetrodotoxin and/or saxitoxin and derivs. thereof, in a pharmaceutically suitable vehicle.

IT **4368-28-9**, Tetrodotoxin
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(method of local anesthesia and analgesia using sodium channel blockers and local anesthetics)
RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



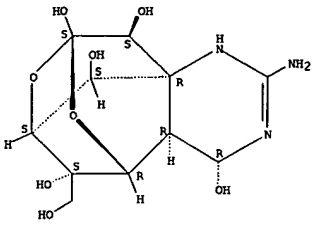
L8 ANSWER 45 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:725238 HCAPLUS
DOCUMENT NUMBER: 138:281020
TITLE: Halothane attenuates the cerebroprotective action of several Na+ and Ca2+ channel blockers via reversal of their ion channel blockade
AUTHOR(S): Oka, Michiko; Itoh, Yoshinori; Fujita, Takuya
CORPORATE SOURCE: Department of Biochemical Pharmacology, Kyoto Pharmaceutical University, Kyoto, Yamashina, 607-8414, Japan
SOURCE: European Journal of Pharmacology (2002), 452(2), 175-181
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The authors have previously shown the involvement of Na+ channel as well as N-type and P/Q-type Ca2+ channels in the oxygen and glucose deprivation-induced injury in rat cerebrocortical slices. In the present study, the authors investigated the influence of halothane on the cerebroprotective effects of a variety of Na+ and Ca2+ channel blockers in rat cerebrocortical slices. The hypoxic injury was attenuated by Na+ channel blockers including tetrodotoxin, lidocaine, and dibucaine, and Ca2+ channel blockers, such as verapamil, ω-agatoxin IVA, and ω-conotoxin GVIA. Halothane abolished the protective effects of lidocaine, dibucaine, and verapamil, all of which block the resp. cation channels in a voltage-dependent manner, without affecting the actions of tetrodotoxin, ω-agatoxin IVA, and ω-conotoxin GVIA, which reveal voltage-independent blockade. On the other hand, the NO synthesis estimated from the extracellular cyclic GMP formation was elevated during exposure to hypoxia. All channel blockers tested here attenuated hypoxia-evoked NO synthesis. Halothane blocked almost completely these actions of lidocaine and verapamil. Moreover, the Na+ and Ca2+ channel blockade by these compds., as determined by veratridine- and KCl-stimulated NO synthesis, resp., was also reversed by halothane. These findings suggest that an anesthetic agent halothane reversed the Na+ and Ca2+ channel blockade of several voltage-dependent ion channel blockers, leading to the attenuation of their cerebroprotective actions. Therefore, the influence of halothane anesthesia should be taken into consideration for the evaluation of neuroprotective action of Na+ and Ca2+ channel blockers.

IT **4368-28-9**, Tetrodotoxin
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(halothane on cerebroprotective effects of Na+ and Ca2+ channel blockers)
RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L8 ANSWER 45 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)



REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 46 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:408544 HCAPLUS
DOCUMENT NUMBER: 136:406875
TITLE: Pharmaceutical injections containing sodium channel blocking compounds
INVENTOR(S): Kang, Yuhong; Shum, Frank Haykong
PATENT ASSIGNEE(S): Nanning Maple Leaf Pharmaceutical Co., Ltd., Peop. Rep. China
SOURCE: PCT Int. Appl., 60 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002041915	A1	20020530	WO 2001-CN1566	20011119
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CN 1353990	A	20020619	CN 2000-132672	20001122
US 2002119987	A1	20020829	US 2001-819796	20010329
US 6559154	B2	20030506		
AU 2002021491	A5	20020603	AU 2002-21491	20011119
EP 1335747	A1	20030820	EP 2001-997312	20011119
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004513186	T2	20040430	JP 2002-544092	20011119

PRIORITY APPLN. INFO.: CN 2000-132672 A 20001122
WO 2001-CN1566 W 20011119

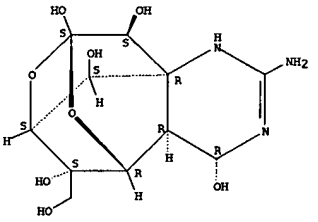
AB The composition of the present invention comprises a sodium channel blocking compound which is capable of specifically binding to a site, either on an SS1 region or an SS2 region, on an extracellular region of a sodium channel alpha subunit, and a pharmaceutically acceptable carrier. An injection contained tetrodotoxin 1.5, 0.5% acetic acid 0.1, propylene glycol 80, and water for injection 100 mL. Stability of tetrodotoxin against light, heat, and storage time was studied.

IT **4368-28-9**, Tetrodotoxin
RL: PRP (Properties); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(pharmaceutical injections containing sodium channel blocking compds.)

RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L8 ANSWER 46 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

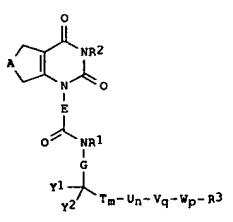
L8 ANSWER 47 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:366971 HCAPLUS
DOCUMENT NUMBER: 136:386124
TITLE: Preparation of amidoalkyluracils as inhibitors of poly(ADP-ribose)synthetase (PARS)
INVENTOR(S): Albrecht, Barbara; Gerisch, Michael; Handke, Gabriele; Jensen, Axel; Krahn, Thomas; Nickl, Werner; Oehme, Felix; Schlemmer, Karl-Heinz; Steinhagen, Henning
PATENT ASSIGNEE(S): Bayer Ag, Germany
SOURCE: Ger. Offen., 70 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 10056312	A1	20020516	DE 2000-10056312	20001114
CA 2428335	AA	20020523	CA 2001-2428335	20011102
WO 2002040455	A1	20020523	WO 2001-EP12694	20011102
WO 2002040455	C1	20020718		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002024825	A5	20020527	AU 2002-24825	20011102
EP 1339699	A1	20030903	EP 2001-994632	20011102
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2005075347	A1	20050407	US 2003-416622	20031229

PRIORITY APPLN. INFO.: DE 2000-10056312 A 20001114
WO 2001-EP12694 W 20011102

OTHER SOURCE(S): MARPAT 136:386124
GI



AB Title compds. [I; A = D, CH2D, DCH2, CH:CHCH2, CH2CH:CH, CH2CH2D, DCH2CH2, CH2DCH2; D = CH2, O, S; E, G = (substituted) alkylene, cycloalkylene; T =

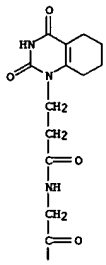
L8 ANSWER 47 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)
CH2; U, V = (substituted) aryl, heterocyclyl; W = O, S, CO2, OCO, NR4; R4 = H, alkyl; m, n, q, p = 0, 1; X = O, S, NR5; R5 = H, alkyl, PhCH2; Y1 = H; Y2 = OH; Y1Y2 = O, S, NR6; R6 = H, alkyl, PhCH2; R1 = H, alkyl, (halo)cycloalkyl; R2 = H, alkoxycarbonyl; R3 = (substituted) aryl, heterocyclyl] were prepd. Thus, a mixt. of 3-(2,4-dioxo-3,4,5,6,7,8-hexahydro-1(2H)-quinazolinyl)propanoic acid (prepn. given) and 2-(2-naphthyl)-2-oxo-1-ethanamine hydrochloride in CH2Cl2 was treated with diisopropylamine and 4-dimethylaminopyridine, followed by addn. of 1,3-dicyclohexylcarbodiimide at 0° and stirring for 18 h at room temp., to give 48% 3-(2,4-dioxo-3,4,5,6,7,8-hexahydro-1(2H)-quinazolinyl)-N-[2-(2-naphthyl)-2-oxo-1-ethyl]propanamide. Several I inhibited PARS with IC50 = 8.5-80 nM.

IT **425635-30-9P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of amidoalkyluracils as inhibitors of poly(ADP-ribose)synthetase (PARS))

RN 425635-30-9 HCAPLUS

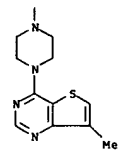
CN 1(2H)-Quinazolinepropanamide, 3,4,5,6,7,8-hexahydro-N-[2-[4-(7-methylthieno[3,2-d]pyrimidin-4-yl)-1-piperazinyl]-2-oxoethyl]-2,4-dioxo-(9CI) (CA INDEX NAME)

PAGE 1-A



L8 ANSWER 47 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 2-A



L8 ANSWER 48 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:293656 HCAPLUS
DOCUMENT NUMBER: 136:325565
TITLE: Preparation of 3,4-dihydropyrimido[1,2-a]pyrimidines and 3,4-dihydropyrazino[1,2-a]pyrimidines as analgesics
INVENTOR(S): Gerlach, Matthias; Maul, Corinna; Jagusch, Utz-Peter
PATENT ASSIGNEE(S): Gruenenthal Gmbh, Germany
SOURCE: PCT Int. Appl., 60 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002030934	A1	20020418	WO 2001-EP11702	20011010
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10050661	A1	20020418	DE 2000-10050661	20001013
AU 2002014007	A5	20020422	AU 2002-14007	20011010
CA 2425685	AA	20030411	CA 2001-2425685	20011010
EP 1325010	A1	20030709	EP 2001-982417	20011010
EP 1325010	B1	20050427		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001014735	A	20031014	BR 2001-14735	20011010
JP 2004511485	T2	20040415	JP 2002-534320	20011010
NZ 525651	A	20041029	NZ 2001-525651	20011010
AT 294180	E	20050515	AT 2001-982417	20011010
ES 2239168	T3	20050916	ES 2001-1982417	20011010
NO 2003001588	A	20030408	NO 2003-1588	20030408
US 2003220322	A1	20031127	US 2003-409614	20030409
ZA 2003003634	A	20040812	ZA 2003-3634	20030512
HK 1056558	A1	20051216	HK 2003-108915	20031209

PRIORITY APPLN. INFO.: DE 2000-10050661 A 20001013
WO 2001-EP11702 W 20011010

OTHER SOURCE(S): MARPAT 136:325565
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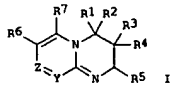


I

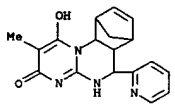
AB Title compds. [I; Y = CR8; Z = N; or Y = N; Z = CR9; R1, R2 = H,

L8 ANSWER 48 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)
(branched) (unsatd.) (substituted) alkyl, (unsatd.) (substituted) cycloalkyl, (unsatd.) (substituted) heterocyclyl, (substituted) (hetero)aryl, (substituted) alkylaryl, etc.; R3, R4 = H, H, (branched) (unsatd.) (substituted) alkyl, (unsatd.) (substituted) cycloalkyl, (substituted) (hetero)aryl, (substituted) alkylaryl, etc.; R5 = (branched) (unsatd.) (substituted) alkyl, (unsatd.) (substituted) cycloalkyl, (unsatd.) (substituted) heterocyclyl, (substituted) (hetero)aryl, (substituted) alkylaryl, etc.; R6-R9 = H, F, Cl, Br, iodo, cyano, amino, aminoalkyl, aminodialkyl, etc.] and salts thereof were prepd. Several I showed μ-opiate receptor binding with Ki = 1.4-2.5 μM and inhibited at 10 μM NMDA/MK801 binding position with 40-47%. The invention relates also to a method for the prodn. of the title compds., substance libraries contg. said compds., medicaments which contain said compds., the use of said compds. in the prodn. of medicaments for treating pain, urinary incontinence, pruritus, tinnitus aurium and/or diarrhea and pharmaceutical prepns. contg. said compds.

IT **412350-23-3P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of dihydropyrimidopyrimidines and dihydropyrazinopyrimidines as analgesics)

RN 412350-23-3 HCAPLUS

CN 7,10-Methano-3H-pyrimido[1,2-a]quinazolin-3-one, 4,6,6a,7,10,10a-hexahydro-1-hydroxy-2-methyl-6-(2-pyridinyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 49 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:220374 HCAPLUS
DOCUMENT NUMBER: 136:241691
TITLE: A method of analgesia using sodium channel blockers
INVENTOR(S): Dong, Qingbin; Shum, Frank Haykong
PATENT ASSIGNEE(S): WEX Medical Instrumentation Co., Peop. Rep. China
SOURCE: PCT Int. Appl., 60 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002022129	A1	20020321	WO 2001-CN1391	20010911
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CN 1356104	A	20020703	CN 2000-124517	20000918
US 6407088	B1	20020618	US 2000-695053	20001025
CA 2421562	AA	20020321	CA 2001-2421562	20010911
AU 2002013785	A5	20020326	AU 2002-13785	20010911
EP 1320369	A1	20030625	EP 2001-982091	20010911
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001013961	A	20040113	BR 2001-13961	20010911
JP 2004508404	T2	20040318	JP 2002-526380	20010911
EE 200300106	A	20050415	EE 2003-106	20010911
EP 1563839	A1	20050817	EP 2004-22073	20010911
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, LT, LV, FI, MK, CY, AL, TR				
NO 2003000915	A	20030425	NO 2003-915	20030227
ZA 2003001852	A	20040621	ZA 2003-1852	20030306
BG 107690	A	20040130	BG 2003-107690	20030331

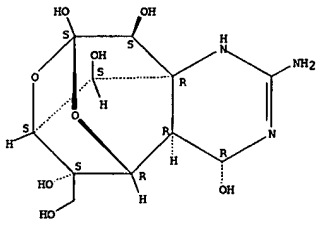
PRIORITY APPLN. INFO.:
CN 2000-124517 A 20000918
EP 2001-982091 A3 20010911
WO 2001-CN1391 W 20010911

AB This invention relates to a method of producing analgesia in a mammal experiencing pain by systemically administering an effective amount of a composition comprising essentially of a sodium channel blocking compound, in a suitable pharmaceutical vehicle, to alleviate the pain.

IT 4368-28-9, Tetrodotoxin
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(analgesia using sodium channel blockers for neuropathic and cancer pain)

RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 50 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:220373 HCAPLUS
DOCUMENT NUMBER: 136:226808
TITLE: A method of local anesthesia and analgesia using sodium channel blockers and local anesthetics
INVENTOR(S): Ku, Baoshan; Qi, Shiquan
PATENT ASSIGNEE(S): WEX Medical Instrumentation Co., Ltd., Peop. Rep. China
SOURCE: PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002022128	A1	20020321	WO 2001-CN1390	20010911
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CN 1343491	A	20020410	CN 2000-124518	20000918
US 6599906	B1	20030729	US 2000-702826	20001101
AU 2002013784	A5	20020326	AU 2002-13784	20010911

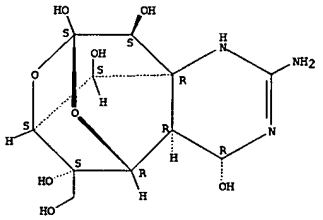
PRIORITY APPLN. INFO.:
CN 2000-124518 A 20000918
WO 2001-CN1390 W 20010911

AB The present invention provides a method of producing local analgesia and anesthesia in a mammal experiencing pain in a nerve tissue region. The method includes topically administering to the region, in a suitable pharmaceutical vehicle, an ED of a sodium channel blocking compound in a pharmaceutically suitable vehicle.

IT 4368-28-9, Tetrodotoxin
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(local anesthesia and analgesia using sodium channel blockers and local anesthetics for neuropathic pain)

RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

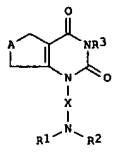


REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 51 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:72062 HCAPLUS
DOCUMENT NUMBER: 136:134774
TITLE: Preparation of fused amidoalkyluracils as poly(ADP-ribose) synthetase inhibitors
INVENTOR(S): Haerter, Michael; Albrecht, Barbara; Gerisch, Michael; Handke, Gabriele; Huetter, Joachim; Jensen, Axel; Krahn, Thomas; Mittendorf, Joachim; Oehme, Felix; Schlemmer, Karl-Heinz; Steinhagen, Henning
PATENT ASSIGNEE(S): Bayer Aktiengesellschaft, Germany
SOURCE: PCT Int. Appl., 113 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002006247	A1	20020124	WO 2001-EP7670	20010705
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
DE 10034801	A1	20020131	DE 2000-10034801	20000718
CA 2416036	AA	20020124	CA 2001-2416036	20010705
EP 1303497	A1	20030423	EP 2001-947443	20010705
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2003022905	A1	20030130	US 2001-906296	20010716
US 6649618	B2	20031118		
PRIORITY APPLN. INFO.:			DE 2000-10034801 A	20000718
			WO 2001-EP7670 W	20010705
OTHER SOURCE(S):	MARPAT 136:134774			

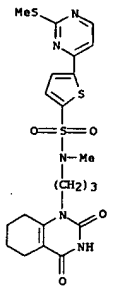
GI



AB Title compds. [I; A = D, CH2D, DCH2, CH:CHCH2, CH2CH:CH, CH2CH2D, DCH2CH2, CH2DCH2; D = CH2, O, S; X = (substituted) alkylene, cycloalkylene; R1 = H, (halogenated) alkyl, cycloalkyl; R2 = SO2R4, SO2NR5R6, COR7, CONR8R9, CO2R10; R4 = (substituted) alkyl, cycloalkyl, GE; E = (substituted) aryl, heterocyclyl, G is absent or (substituted) aryl, heteroaryl; R5, R6 = H, (substituted) cycloalkyl, alkyl, aryl, heteroaryl; or R5R6 = (substituted) heterocyclyl; R7 = (substituted) alkyl, cycloalkyl; GE (as above); R8, R9 = H, (substituted) alkyl, cycloalkyl; or R8R9 = (substituted) heteroaryl; R10 = (substituted) alkyl, cycloalkyl, aryl; or R1R2 = (substituted) mono- or bicyclic heterocyclyl; R3 = H, alkoxycarbonyl], were prepd. Thus, a mixt. of N-(3-aminopropyl)-N-benzyl-N-methylamine and tetrahydro-4H-thiopyran-4-one in PhMe was refluxed with camphorsulfonic acid followed by addn. of ClCONCO at room temp. to give 67% 1-[3-benzyl(methyl)aminopropyl]-1,5,7,8-tetrahydro-2H-thiopyrano[4,3-d]pyrimidine-2,4(3H)-dione which was stirred with 2,2,2-trichloroethylchloroformate in MeCN for 30 min at room temp. to give 63% 2,2,2-trichloroethyl-3-(2,4-dioxo-3,4,7,8-tetrahydro-2H-thiopyrano[4,3-d]pyrimidin-1(5H)-yl)propyl(methyl)carbamate. Tested I showed 50% protection of endothelial cells with EC50 = 0.05-0.5 μM.

IT **390766-30-0P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of fused amidoalkyluracils as poly(ADP-ribose) synthetase inhibitors)

RN 390766-30-0 HCAPLUS
CN 2-Thiophenesulfonamide, N-[3-(3,4,5,6,7,8-hexahydro-2,4-dioxo-1(2H)-quinazolinyl)propyl]-N-methyl-5-[2-(methylthio)-4-pyrimidinyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

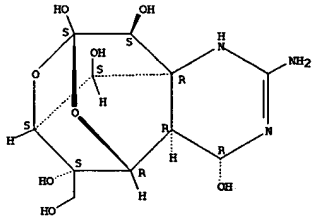
L8 ANSWER 52 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:750642 HCAPLUS
DOCUMENT NUMBER: 135:284379
TITLE: β-scorpion toxin induces the release of γ-[3H]aminobutyric acid in rat brain slices
AUTHOR(S): Fernandes, V. M. V.; Nicolato, R.; Moraes-Santos, T.; Gomez, R. S.; Prado, M. A. M.; Romano-Silva, M. A.; Gomez, M. V.
CORPORATE SOURCE: Laboratorio de Neurofarmacologia, Departamento de Farmacologia, Faculdade de Farmacia, ICB-UFMG, Belo Horizonte, 31270-901, Brazil
SOURCE: NeuroReport (2001), 12(13), 2911-2913
CODEN: NERPEZ; ISSN: 0959-4965
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The effect of the β-scorpion toxin, TiTX γ on the release of [3H]GABA from rat brain cortical slices is described. The stimulatory effect of TiTX γ on the release of [3H]GABA was dependent on incubation time and TiTX γ concentration with an EC50 of 0.19 μM. The scorpion toxin effect was Ca dependent and was completely inhibited by tetrodotoxin. β-Alanine also induced the release of [3H]GABA and this effect was not inhibited by tetrodotoxin but was additive in the presence of TiTX γ. The data suggest a neuronal origin for the release of [3H]GABA by TiTX γ.

IT **4368-28-9**, Tetrodotoxin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(β-scorpion toxin induced release of γ-aminobutyric acid in rat brain inhibition by tetrodotoxin)

RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 53 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:748770 HCAPLUS
DOCUMENT NUMBER: 136:79620
TITLE: Time course studies on the effectiveness of tetrodotoxin in reducing consequences of spinal cord contusion
AUTHOR(S): Rosenberg, Lisa J.; Wrathall, Jean R.
CORPORATE SOURCE: Department of Neuroscience, Georgetown University, Washington, DC, 20007, USA
SOURCE: Journal of Neuroscience Research (2001), 66(2), 191-202
CODEN: JNREDK; ISSN: 0360-4012
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

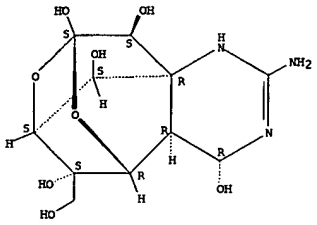
AB Focal injection of the sodium channel blocker tetrodotoxin (TTX) into the injury site at either 5 or 15 min after a standardized thoracic contusion spinal cord injury (SCI) reduces white matter pathol. and loss of axons in the first 24 h after injury. Focal injection of TTX at 15 min after SCI also reduces chronic white matter loss and hindlimb functional deficits. We have now tested the hypothesis that the reduction in chronic deficits with TTX treatment is associated with long-term preservation of axons after SCI and compared both acute (24 h) and chronic (6 wk) effects of TTX administered at 15 min prior to and 5 min or 4 h after SCI. Our results indicate a significant reduction of acute white matter pathol. in rats treated with TTX at 15 min before and 5 min after injury but no effect when treatment was delayed until 4 h after contusion. Compared with injury controls, groups treated with TTX at 5 min and 4 h after injury did not show a significant deficit reduction, nor was there a significant sparing of white matter at 6 wk compared with injury controls. In contrast, the group treated with TTX at 15 min before SCI demonstrated significantly reduced hindlimb functional deficits beginning at 1 wk after injury and throughout the 6 wk of the study. This was associated with a significantly higher axon d. in the ventromedial white matter at 6 wk. The results demonstrate that blockade of sodium channels preserves axons from loss after SCI and points to the importance of time of administration of such drugs for therapeutic effectiveness.

IT **4368-28-9**, Tetrodotoxin
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(time course studies on effectiveness of tetrodotoxin in reducing consequences of spinal cord contusion)

RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L8 ANSWER 53 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)



REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 54 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN

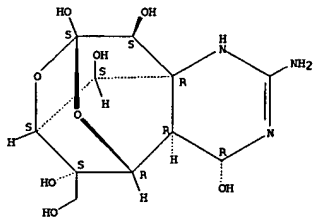
ACCESSION NUMBER: 2001:660029 HCAPLUS
DOCUMENT NUMBER: 136:335125
TITLE: High concentrations of adrenergic antagonists prolong sciatic nerve blockade by tetrodotoxin
AUTHOR(S): Kohane, D. S.; Lu, N. T.; Crosa, G. A.; Kuang, Y.; Berde, C. B.
CORPORATE SOURCE: Department of Anesthesia, Children's Hospital, Boston, MA, USA
SOURCE: Acta Anaesthesiologica Scandinavica (2001), 45(7), 899-905
CODEN: AANEAB; ISSN: 0001-5172
PUBLISHER: Munksgaard International Publishers Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Background: Millimolar-range concns. of some adrenergic antagonists were shown to have local anesthetic-like properties, and to stimulate GTPase activity in vitro. In this report, the authors investigate whether these agents can potentiate the effect of tetrodotoxin (TTX) and bupivacaine, a conventional local anesthetic, and whether GTPase activation plays a role. Methods: Rats received sciatic nerve blockade with tetrodotoxin or bupivacaine co-injected with adrenergic antagonists and/or agonists, or pertussis toxin. Thermal nociceptive blockade was quantified with modified hot-plate testing. Results: Nerve block from TTX alone lasted 153 (99-223) min (median and 25th and 75th percentiles). Co-injection with 20 mM phentolamine, propranolol, and yohimbine prolonged TTX block to 856 (765-862), 486 (444-510), and 465 (413-495) min resp. Micromolar concns. of adrenergic antagonists (which inhibited the prolongation of TTX block by epinephrine) did not prolong TTX block. Injection of adrenergic antagonists alone did not produce specific nerve block. They did not prolong TTX block when injected at a remote s.c. site. Prolongation of TTX block by phentolamine was not inhibited by co-injection with pertussis toxin. Adrenergic antagonists did not prolong bupivacaine block. Conclusions: High concns. of adrenergic antagonists markedly prolonged TTX block, but not bupivacaine block. This locally mediated action does not appear to be adrenergic-receptor-specific, or mediated by GTPase activation.

IT **4368-28-9**, Tetrodotoxin
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(adrenergic antagonists prolong sciatic nerve blockade by tetrodotoxin)
RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L8 ANSWER 54 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)



REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 55 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:566880 HCAPLUS
DOCUMENT NUMBER: 135:134288
TITLE: Diagnostic kit and method and creatine recognizing agents for detecting creatine levels
INVENTOR(S): Al Athel, Fahad Mohammed Saleh; Bell, Thomas W.; Khasanov, Alisher B.; Kaddurah-Daouk, Rima
PATENT ASSIGNEE(S): Fal Diagnostics, USA
SOURCE: PCT Int. Appl., 56 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001055719	A2	20010802	WO 2001-US2650	20010126
WO 2001055719	A3	20011213		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6566086	B1	20030520	US 2000-494205	20000128
PRIORITY APPLN. INFO.:			US 2000-494205 A	20000128
OTHER SOURCE(S):	MARPAT 135:134288			

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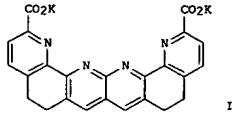

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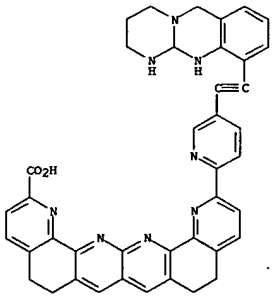
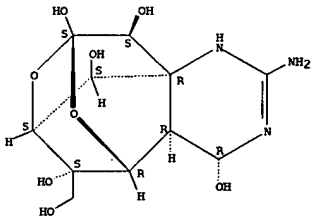
AB Methods for the detection of creatine compound levels in body fluid samples are discussed. Portable kits capable of determining creatine levels using non-invasive and visually detectable methods are also included. I was prepared from quinaldine and used to detect creatine by 1H NMR spectroscopy.

IT **352229-25-5**
RL: ARG (Analytical reagent use); **THU (Therapeutic use)**; ANST (Analytical study); BIOL (Biological study); USES (Uses)
(diagnostic kit and method and creatine recognizing agents for detecting creatine levels)
RN 352229-25-5 HCAPLUS
CN [1,10]Phenanthrolino[2,3-b][1,10]phenanthroline-2-carboxylic acid, 13-[5-[(1,3,4,6,11,11a-hexahydro-2H-pyrimido[2,1-b]quinazolin-10-yl)ethynyl]-2-pyridinyl]-5,6,9,10-tetrahydro- (9CI) (CA INDEX NAME)

L8 ANSWER 55 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)



L8 ANSWER 56 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)



REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 56 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:563098 HCAPLUS
DOCUMENT NUMBER: 137:122
TITLE: A method to evaluate the diffusion rate of drugs from a microdialysis probe through brain tissue
AUTHOR(S): Westerink, B. H. C.; De Vries, J. B.
CORPORATE SOURCE: Department of Biomonitoring and Sensoring, University Centre for Pharmacy, University of Groningen, Groningen, 9713 AV, Neth.
SOURCE: Journal of Neuroscience Methods (2001), 109(1), 53-58
CODEN: JNMEDT; ISSN: 0165-0270
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB For interpretation of microdialysis expts. in which compds. are applied by retrodialysis, it is important to have information about the migration rate of the infused compds. Here we describe a dual-probe microdialysis method that can be used to evaluate the penetration rate of the infused drug. The basic idea is that not the drug itself is assayed, but that its pharmacol. effect is recorded by a second probe positioned at a fixed distance (1 mm) of the infusion probe. Using this approach several compds., each known to induce specific changes in the extracellular levels of dopamine, were infused into the striatum of the rat. The results indicate that the penetration rate of the pharmacol. effect of infused compds. differed widely. No effects were seen at the second probe when high potassium chloride was infused. Apparently dopamine was not able to migrate into brain tissue over a distance of 1 mm. Low penetration rates were observed for the dopamine antagonist sulpiride, the dopamine agonist LY 171555, and for amphetamine and nomifensine. A very high penetration rate was observed in case of tetrodotoxin (TTX). The fast effects of TTX could also be explained by remote inhibition of neurons passing along the infusion probe. The present study showed that most of the compds. have rather slow infusion rates, indicating that relatively high infusion concns. are needed (1-10 mM) to reach substantial brain concns. at a distance of 1 mm from the infusion probe.

IT **4368-28-9**, Tetrodotoxin
RL: PKT (Pharmacokinetics); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(method to evaluate the diffusion rate of drugs from a microdialysis probe through brain tissue)

RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L8 ANSWER 57 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:453494 HCAPLUS
DOCUMENT NUMBER: 135:41024
TITLE: Compositions, kits, apparatus, and methods for inhibiting cephalic inflammation by intranasal administration of long-acting local anesthetic
INVENTOR(S): Levin, Bruce H.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 48 pp., Cont.-in-part of U.S. Ser. No. 118,615.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

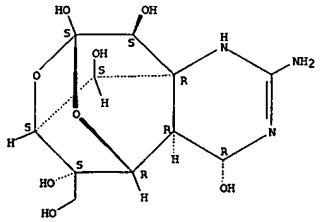
PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2001004644	A1	20010621	US 2000-737302		20001215
US 2001055607	A1	20011227	US 1998-118615		19980717
US 6432986	B2	20020813			
US 2002010194	A1	20020124	US 2001-775724		20010201
US 2003133877	A1	20030717	US 2002-218138		20020812
US 2005281751	A1	20051222	US 2005-126475		20050511
PRIORITY APPLN. INFO.:			US 1997-90110P	P	19970721
			US 1998-72845P	P	19980128
			US 1998-84559P	P	19980506
			US 1998-118615	A2	19980717
			US 1999-170817P	P	19991215
			US 1997-897192	A	19970721
			US 1999-117398P	P	19990127
			US 2000-492946	A2	20000127
			US 2000-737302	B2	20001215
			US 2002-218138	A2	20020812

AB Methods, kits, apparatus, and compns. for inhibiting cephalic inflammation, including meningeal inflammation and cerebral inflammation for example, in a human patient are provided. The methods comprise intranasally administering to the patient a pharmaceutical composition comprising a local anesthetic, and preferably a long-acting local anesthetic ingredient. A composition useful for practicing the methods of the invention is described which comprises at least one local anesthetic in a pharmaceutically acceptable carrier, wherein the composition is formulated for intranasal delivery. A kit comprising the composition and an intranasal applicator is also included in the invention. Apparatus for delivering or applying the compns. of the invention or for performing the methods of the invention are also described. Ropivacaine was dorsonasally administered to individual patients experiencing head pain, other symptoms, or both, believed to be associated with an acute migraine episode. Dorsonasally administered ropivacaine rapidly inhibited of migraine in 92% of the ambulatory patients, as evidenced by an average 90% reduction in perceived pain within one hour, usually within 15 min or less. Symptoms of nausea and photophobia associated with acute migraine episodes in patients were similarly inhibited. Rebound of migraine occurred in only 5.4% of patients within twenty-four hours of treatment.

IT **4368-28-9**, Tetrodotoxin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(compns. and kits and apparatus and methods for inhibiting cephalic inflammation by intranasal administration of long-acting local

L8 ANSWER 57 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)
anesthetic)
RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L8 ANSWER 58 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:452849 HCAPLUS
DOCUMENT NUMBER: 135:56081
TITLE: Compositions, kits, apparatus, and methods for inhibiting cephalic inflammation resulting in acute migraine and other painful episodes associated with neurovascular disorders
INVENTOR(S): Levin, Bruce H.
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 119 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

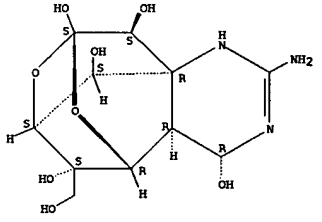
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001043733	A2	20010621	WO 2000-US33916	20001215
WO 2001043733	A3	20020510		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-170817P P 19991215
AB Methods, kits, apparatus, and compns. for inhibiting cephalic inflammation, including meningeal inflammation and cerebral inflammation for example, in a human patient are provided. The treatment is for acute cerebral neurovascular disorders resulting in acute migraine and other painful episodes. The methods comprise intranasally administering to the patient a pharmaceutical composition comprising a local anesthetic, and preferably a long-acting local anesthetic ingredient. A composition useful for practicing the methods of the invention is described which comprises at least one local anesthetic in a pharmaceutically acceptable carrier, wherein the composition if formulated for intranasal delivery. A kit comprising the composition and an intranasal applicator is also included in the invention. Apparatus for delivering or applying the compns. of the invention or for performing the methods of the invention are also described.
IT **4368-28-9**, Tetrodotoxin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(compns., kits, apparatus, and methods for inhibiting cephalic inflammation resulting in acute migraine and other painful episodes associated with neurovascular disorders)
RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-,

L8 ANSWER 58 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)
(4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

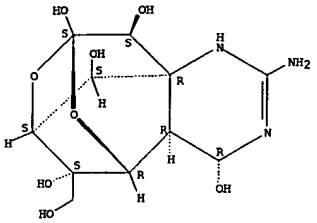
Absolute stereochemistry.



L8 ANSWER 59 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:454869 HCAPLUS
DOCUMENT NUMBER: 133:232658
TITLE: Inhibition of different pathways influencing Na+ homeostasis protects organotypic hippocampal slice cultures from hypoxic/hypoglycemic injury
AUTHOR(S): Breder, J.; Sabelhaus, C. F.; Opitz, T.; Reymann, K. G.; Schroder, U. H.
CORPORATE SOURCE: Project Group Neuropharmacology, Leibniz Institute for Neurobiology, Magdeburg, D-39008, Germany
SOURCE: Neuropharmacology (2000), 39(10), 1779-1787
CODEN: NEPHBW; ISSN: 0028-3908
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A prominent feature of cerebral ischemia is the excessive intracellular accumulation of both Na+ and Ca2+, which results in subsequent cell death. A large number of studies have focused on pathways involved in the increase of the intracellular Ca2+ concentration [Ca2+]i, whereas the elevation of intracellular Na+ has received less attention. In the present study we investigated the effects of inhibitors of different Na+ channels and of the Na+/Ca2+ exchanger, which couples the Na+ to the Ca2+ gradient, on ischemic damage in organotypic hippocampal slice cultures. The synaptically evoked population spike in the CA1 region was taken as a functional measure of neuronal integrity. Neuronal cell death was assessed by propidium iodide staining. The Na+ channel blocker tetrodotoxin, and the NMDA receptor blocker MK 801, but not the AMPA/kainate receptor blocker NBQX prevented ischemic cell death. The novel Na+/Ca2+ exchange inhibitor 2-[2-[4-(4-nitrobenzyloxy)phenyl]ethyl]isothiourea methanesulfonate (KB-R7943), which preferentially acts on the reverse mode of the exchanger, leading to Ca2+ accumulation, also reduced neuronal damage. At higher concns., KB-R7943 also inhibits Ca2+ extrusion by the forward mode of the exchanger and exaggerates neuronal cell death. Neuroprotection by KB-R7943 may be due to reducing the [Ca2+]i increase caused by the exchanger.
IT **4368-28-9**, Tetrodotoxin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(inhibition of different pathways influencing Na+ homeostasis protects organotypic hippocampal slice cultures from hypoxic/hypoglycemic injury)
RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L8 ANSWER 59 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)



REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 60 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:351162 HCAPLUS
DOCUMENT NUMBER: 133:790
TITLE: New use of glutamate antagonists for the treatment of cancer
INVENTOR(S): Ikonomidou, Hrissanthi
PATENT ASSIGNEE(S): Germany
SOURCE: Eur. Pat. Appl., 21 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1002535	A1	20000524	EP 1998-250380	19981028
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
AU 9964750	A1	20000515	AU 1999-64750	19991022
EP 1124553	A1	20010822	EP 1999-952622	19991022
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002528415	T2	20020903	JP 2000-578005	19991022
EP 1586321	A1	20051019	EP 2005-12871	19991022
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
US 6797692	B1	20040928	US 2001-830354	20010425
US 2005054619	A1	20050310	US 2004-912159	20040806
US 2005054650	A1	20050310	US 2004-912175	20040806

PRIORITY APPLN. INFO.:
EP 1998-250380 A 19981028
EP 1999-952622 A3 19991022
WO 1999-EP8004 W 19991022
US 2001-830354 A3 20010425

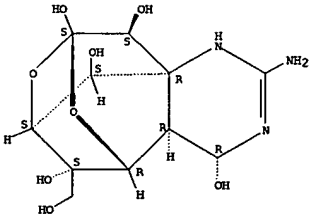
AB New therapies can be devised based upon a demonstration of the role of glutamate in the pathogenesis of cancer. Inhibitors of the interaction of glutamate with the AMPA, kainate, or NMDA receptor complexes are likely to be useful in treating cancer and can be formulated as pharmaceutical compns. They can be identified by appropriate screens.

IT **4368-28-9**, Tetrodotoxin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(glutamate antagonists for cancer treatment)

RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L8 ANSWER 60 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)



REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 61 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:290862 HCAPLUS
DOCUMENT NUMBER: 132:303512
TITLE: Methods for enhancing wound healing
INVENTOR(S): Gassner, Holger G.; Sherris, David A.
PATENT ASSIGNEE(S): Mayo Foundation for Medical Education and Research, USA
SOURCE: PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000024419	A1	20000504	WO 1999-US24182	19991015
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2347828	AA	20000504	CA 1999-2347828	19991015
BR 9914891	A	20010717	BR 1999-14891	19991015
EP 1128844	A1	20010905	EP 1999-960130	19991015
EP 1128844	B1	20060104		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY				
JP 2002528421	T2	20020903	JP 2000-578027	19991015
US 6447787	B1	20020910	US 2001-807793	20010418
US 2003036502	A1	20030220	US 2001-995022	20011126
US 2005175637	A1	20050811	US 2005-61299	20050218
US 2006039930	A2	20060223		

PRIORITY APPLN. INFO.:
US 1998-105688P P 19981027
WO 1999-US24182 W 19991015
US 2001-807793 A3 20010418
US 2001-995022 A1 20011126

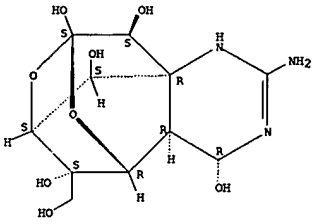
AB A method for treating a patient having a wound is described. The method includes administering an amount of a chemodenervating agent such that healing of the wound is enhanced. The method is illustrated by detailing the mean differences of the scores of the paired exptl. and control scars across three observers. Also claimed is a local administration of compns. containing chemodenervating agents (e.g. botulinum toxins), local anesthetics (e.g. lidocaine), and vasoconstrictors (e.g. epinephrine).

IT **4368-28-9**, Tetrodotoxin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(local administration of compns. containing chemodenervating agents and anesthetics and vasoconstrictors for enhancing wound healing)

RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

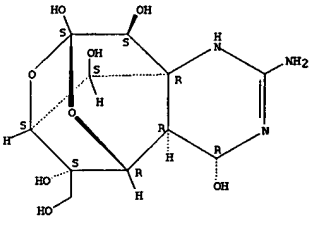
L8 ANSWER 61 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 62 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)
(4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 62 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2000:229542 HCAPLUS
DOCUMENT NUMBER: 132:288238
TITLE: Organotypic hippocampal slice cultures as an in vitro model for the investigation of neuroprotective drugs against ischemic damage
AUTHOR(S): Breder, Jorg; Sabelhaus, Clemens F.; Schroder, Ulrich H.; Reymann, Klaus G.
CORPORATE SOURCE: Laboratory of Neuropharmacology, Leibniz Institute for Neurobiology, Magdeburg, 39008, Germany
SOURCE: Schriften des Forschungszentrums Juelich, Lebenswissenschaften/Life Sciences (1999), 3(Cell Culture Models as Alternatives to Animal Experimentation for the Testing of Neuroprotective Compounds in Stroke Research), 79-98
CODEN: SFLSF9; ISSN: 1433-5549
PUBLISHER: Forschungszentrum Juelich GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Cerebral ischemia results in severe cell degeneration and consequently in loss of brain functions. In animal models of global ischemia the hippocampus has turned out to be 1 of the most vulnerable brain areas, and within the hippocampus the pyramidal neurons of the CA1 region are highly susceptible. These in vivo test systems cause substantial stress in form of pain and anxiety to the animals involved, giving rise to ethical problems and little public acceptance. In vitro models were developed to overcome these problems. Dissociated cell cultures allow the strict control over environmental conditions and easy accessibility to manipulations but suffer from lacking the native neuronal circuitry as it is found in vivo. This major disadvantage can be at least partially circumvented by utilizing organotypic brain slice cultures. Organotypic cultures allow the investigation of delayed pathol. processes after hypoxic/hypoglycemic insults and of the long-term effects of neuroprotective compds. In the present report the authors describe the development of organotypic hippocampal slice cultures maintained on membrane filter inserts at the interface between tissue culture medium and atmospheric as an in vitro model for the investigation of neuroprotective drugs against ischemic damage. Ischemia was simulated in vitro by combined oxygen/glucose deprivation. Neuronal cell death as measured by propidium iodide uptake 24 h after the insult was compared with functional damage as estimated in the short-term range by electrophysiol. recordings of field potentials. Pharmacol. validation was achieved by testing the effects of cytoprotective compds. with different effector mechanisms. Bearing in mind that OSC prepared from neonate rats may not represent the situation found in the adult CNS, they provide an exptl. in vitro system that is well suited to complement in vivo prepns. and dissociated cell cultures in studying long-term pathophysiol. processes of neurodegenerative diseases.

IT **4368-28-9**, TTX
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(protection of organotypic hippocampal slice cultures from ischemic injury)

RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-,

L8 ANSWER 63 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2000:74515 HCAPLUS
DOCUMENT NUMBER: 133:589
TITLE: Neuroprotection against ischemia by metabolic inhibition revisited: A comparison of hypothermia, a pharmacologic cocktail and magnesium plus mexiletine
AUTHOR(S): Maynard, Kenneth I.; Quinones-Hinojosa, Alfredo; Malek, Junaid Y.
CORPORATE SOURCE: Neurophysiology Laboratory, Massachusetts General Hospital and Harvard Medical School, Boston, MA, 02114, USA
SOURCE: Annals of the New York Academy of Sciences (1999), 890(Neuroprotective Agents), 240-254
CODEN: ANYAA9; ISSN: 0077-8923
PUBLISHER: New York Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English

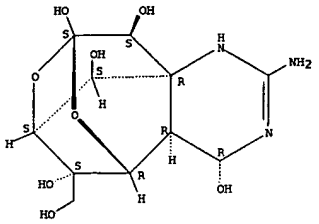
AB Previous studies have suggested that metabolic inhibition is neuroprotective, but little evidence has been provided to support this proposal. Using the in vitro rabbit retina preparation as an established model of the central nervous system (CNS), the authors measured the rate of glucose utilization and lactate production, and the light-evoked compound action potentials (CAPs) as indexes of neuronal energy metabolism and electrophysiol. function, resp. The authors examined the effect of three (3) treatments options: hypothermia (i.e., 33° and 30°), a six-member pharmacol. "cocktail" (tetrodotoxin (0.1 μM), 2-amino-4-phosphonobutyric acid (20 μM), 2-amino-5-phosphonovaleric acid (1 mM), amiloride (1 mM), magnesium (10 mM) and lithium (10 mM)) and the combination of magnesium (Mg^{2+} 1 mM) and mexiletine (Mex, 300 μM) on in vitro rabbit retinas, to see if there is a correlation between neuronal energy metabolism during ischemia (simulated by the reduction of oxygen from 95% to 15% and glucose from 6 mM to 1 mM), and the subsequent recovery of function. Hypothermia and the "cocktail" significantly inhibited both the rate of glucose utilization and lactate production, whereas Mg^{2+} and/or Mex showed only a nonsignificant tendency toward a reduction, compared to control retinas. Recovery of light-evoked CAPs was significantly improved in hypothermia- and cocktail-treated retinas, as well as with retinas exposed to the combination of Mg^{2+} plus Mex, but not with Mg^{2+} or Mex alone, relative to control retinas. A linear regression anal. of the % recovery of function vs. the % reduction in the rate of glucose utilization during ischemia showed a significant correlation (r^2 = 0.80, correlation coefficient = 0.9) between these two parameters. This and other data discussed provide convincing evidence that there is a correlation between metabolic inhibition, achieved during ischemia, and neuroprotection.

IT **4368-28-9**, Tetrodotoxin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(neuroprotection against ischemia by metabolic inhibition revisited and a comparison of hypothermia and pharmacol. cocktail and magnesium plus mexiletine)

RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

L8 ANSWER 63 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)

Absolute stereochemistry.



REFERENCE COUNT: 67 THERE ARE 67 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 64 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN

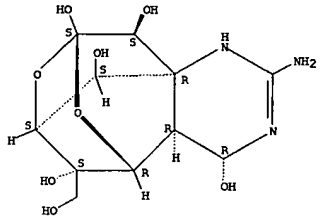
ACCESSION NUMBER: 2000:74167 HCAPLUS
DOCUMENT NUMBER: 132:206290
TITLE: Role of the enteric nervous system in the fluid and electrolyte secretion of rotavirus diarrhea
AUTHOR(S): Lundgren, Ove; Peregrin, Attila Timar; Persson, Kjell; Kordasti, Shirin; Uhnoo, Ingrid; Svensson, Lennart
CORPORATE SOURCE: Department of Physiology, Goteborg University, Goteborg, S-405 30, Swed.
SOURCE: Science (Washington, D. C.) (2000), 287(5452), 491-495
CODEN: SCIEAS; ISSN: 0036-8075
PUBLISHER: American Association for the Advancement of Science
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The mechanism underlying the intestinal fluid loss in rotavirus diarrhea, which often afflicts children in developing countries, is not known. One hypothesis is that the rotavirus evokes intestinal fluid and electrolyte secretion by activation of the nervous system in the intestinal wall, the enteric nervous system (ENS). 4 Different drugs that inhibit ENS functions were used to obtain exptl. evidence for this hypothesis in mice in vitro and in vivo. The involvement of the ENS in rotavirus diarrhea indicates potential sites of action for drugs in the treatment of the disease.

IT **4368-28-9**, Tetrodotoxin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); ~~THU~~ (Therapeutic use); BIOL (Biological study); USES (Uses)
(enteric nervous system in the fluid and electrolyte secretion in rotavirus diarrhea)

RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 65 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2000:14313 HCAPLUS
DOCUMENT NUMBER: 132:276201
TITLE: Long-term myocardial preservation: beneficial and additive effects of polarized arrest (Na+-channel blockade), Na+/H+-exchange inhibition, and Na+/K+/2Cl--cotransport inhibition combined with calcium desensitization
AUTHOR(S): Snabaitis, Andrew K.; Chambers, David J.
CORPORATE SOURCE: Cardiovascular Research, The Rayne Institute, St Thomas Hospital, London, SE1 7EH, UK
SOURCE: Transplantation (1999), 68(10), 1444-1453
CODEN: TRPLAU; ISSN: 0041-1337
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

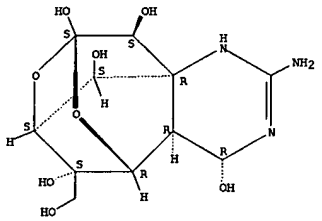
AB Background: Polarized arrest, induced by tetrodotoxin (TTX) at an optimal concentration of 22 μmol/L, has been shown to reduce ionic imbalance and improve myocardial preservation compared with hyperkalemic (depolarized) arrest. Addnl. pharmacol. manipulation of ionic changes (involving inhibition of Na+ influx by the Na+/H+ exchanger [HOE694] and Na+/K+/2Cl- cotransporter [furosemide], and calcium desensitization [BDM]) may further improve long-term preservation. In this study, we (i) established optimal concns. of each drug, (ii) determined additive effects of optimal concns. of each drug and (iii) compared our optimal preservation solution to an established depolarizing cardioplegia (St Thomas' Hospital solution No 2: STH2) used during long-term hypothermic storage for clin. transplantation. Methods: The isolated working rat heart, perfused with Krebs Henseleit (KH) buffer was used; cardiac function was measured after 20 min aerobic working mode perfusion. The hearts (n=6/group) were arrested with a 2 mL infusion (for 30 s) of the polarizing (control) solution (22 μmol/L TTX in KH) or control+drug and subjected to 5 h or 8 h of storage at 7.5°C in the arresting solution Postischemic function during reperfusion was measured (expressed as percentage of preischemic function). Results: Dose-response studies established optimal concns. of HOE694 (10 μmol/L), furosemide (1.0 μmol/L) and BDM (30 mmol/L) in the polarizing (control) solution Sequential addition to the control solution (Group I) of optimal concns. of HOE694 (Group II), furosemide (Group III), and BDM (Group IV) were compared with STH2 (Group V); postischemic recovery of aortic flow was 29±7%, 49±6%*, 56±2%*, 76±3%*, and 25±6%, resp. (*P<0.05 vs. I and V). Creatine kinase leakage was lowest, and myocardial ATP content was highest in Group IV. Conclusions: A polarizing preservation solution (KH+TTX) containing HOE694, furosemide, and BDM significantly enhanced long-term preservation compared with an optimized depolarizing solution (STH2) used clin. for long-term donor heart preservation.

IT **4368-28-9**, Tetrodotoxin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); ~~THU~~ (Therapeutic use); BIOL (Biological study); USES (Uses)
(sodium channel inhibitor; beneficial effects of polarized arrest (Na+-channel blockade), Na+/H+-exchange inhibition and Na+/K+/2Cl--cotransport inhibition combined with calcium desensitization on long-term heart preservation)

RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L8 ANSWER 65 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)



REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 66 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:715350 HCAPLUS
DOCUMENT NUMBER: 131:317714
TITLE: Morphine contracts the guinea pig ileal circulating muscle by interfering with a nitric oxide mediated tonic inhibition
AUTHOR(S): Lenard, Laszlo, Jr.; Halmai, Vilmos; Bartho, Lorand
CORPORATE SOURCE: Dep. Pharmacology Pharmacotherapy, Medical School, Univ. Pecs, Pecs, H-7643, Hung.
SOURCE: Digestion (1999), 60(6), 562-566
CODEN: DIGEBW; ISSN: 0012-2823
PUBLISHER: S. Karger AG
DOCUMENT TYPE: Journal
LANGUAGE: English

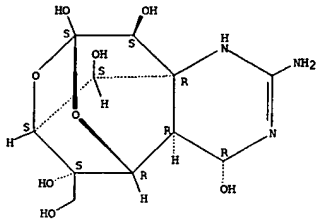
AB The effect of morphine was examined on the circular muscle of guinea pig ileal segments in vitro, with special regard to its interaction with enteric NO releasing neurons. In the presence of atropine (10-6 M), morphine (10-6 M) caused tonic contraction (approx. 7% of the maximal spasm) which was reversed by naloxone (10-6M). Tetrodotoxin (TTX; 10-6 M) also caused contraction (14% of maximum); morphine completely lost its effect in the presence of TTX. Likewise, the NO synthase inhibitor NG-nitro-L-Arg (L-NOARG, 10-4 M) elicited a tonic circular muscle contraction (12% of maximum) and completely prevented the excitatory action of TTX or morphine. The NO donor Na nitro prusside (10-7-10-4 M) caused relaxation. In longitudinally oriented prepns. in the presence of atropine (10-6 M), no change in tone was observed upon administration of morphine (10-6 M), TTX (10-6 M), or L-NOARG (10-4 M). In the circular muscle in the absence of atropine, cholecystokinin octapeptide (CCK-8; 10-9 M) evoked a tonic-phasic contractile response which spontaneously faded away within 3 min. L-NOARG (10-4 M) failed to affect intensity or duration of the response to CCK-8. It is concluded that NO-releasing myenteric neurons exert a tonic inhibitory influence upon the circular, but not longitudinal muscle of the guinea pig ileum. Morphine and TTX probably contract the circular muscle by reducing the amount of NO released. A release of NO seems to play no role in the contractile effect of CCK-8 or in its spontaneous termination.

IT 4368-28-9, Tetrodotoxin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(TTX and morphine effects on the ileal circulating muscle by interfering with a NO mediated tonic inhibition)

RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L8 ANSWER 66 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)



REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 67 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:551459 HCAPLUS
DOCUMENT NUMBER: 132:117410
TITLE: Tetrodotoxin prevents posttraumatic epileptogenesis in rats
AUTHOR(S): Graber, Kevin D.; Prince, David A.
CORPORATE SOURCE: Department of Neurology and Neurological Sciences, Stanford University Medical Center, Stanford, CA, 94305-5300, USA
SOURCE: Annals of Neurology (1999), 46(2), 234-242
CODEN: ANNED3; ISSN: 0364-5134
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

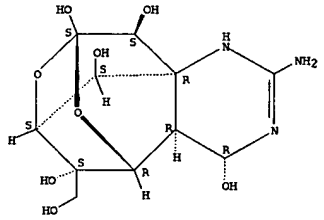
AB Severe cortical trauma frequently causes epilepsy that develops after a long latency. We hypothesized that plastic changes in excitability during this latent period might be initiated or sustained by the level of neuronal activity in the injured cortex. We therefore studied effects of action potential blockade by application of tetrodotoxin (TTX) to areas of cortical injury in a model of chronic epileptogenesis. Partially isolated islands of sensorimotor cortex were made in 28- to 30-day-old male Sprague-Dawley rats and thin sheets of Elvax polymer containing TTX or control vehicle were implanted over lesions. Ten to 15 days later neocortical slices were obtained through isolates for electrophysiol. studies. Slices from all animals (n = 12) with lesions contacted by control-Elvax (58% of 36 slices) exhibited evoked epileptiform field potentials, and those from 4 rats had spontaneous epileptiform events. Only 2 of 11 lesioned animals and 6% of slices from cortex exposed to TTX in vivo exhibited evoked epileptiform potentials, and no spontaneous epileptiform events were observed. There was no evidence of residual TTX during recordings. TTX-Elvax was ineffective in reversing epileptogenesis when implanted 11 days after cortical injury. These data suggest that development of anti-epileptogenic drugs for humans may be possible.

IT 4368-28-9, Tetrodotoxin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(tetrodotoxin prevents posttraumatic epileptogenesis in rats)

RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L8 ANSWER 67 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)



REFERENCE COUNT: 70 THERE ARE 70 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 68 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:465416 HCAPLUS
DOCUMENT NUMBER: 132:102575
TITLE: Effects of tetrodotoxin and OKY-046 in renal ischemia reperfusion
AUTHOR(S): Garvin, Paul J.; Niehoff, Michael L.; Robinson, Sandra M.
CORPORATE SOURCE: Department of Surgery, Abdominal Organ Transplant Division, St. Louis University Health Sciences Center, St. Louis, MO, 63110-0250, USA
SOURCE: Journal of Surgical Research (1999), 85(2), 273-278
CODEN: JSGRA2; ISSN: 0022-4804
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English

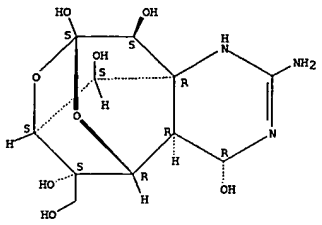
AB Ischemia reperfusion injury (IRI) contributes significantly to posttransplant graft dysfunction. An emphasis, therefore, has been directed toward the identification of novel renoprotective agents. In this study, the renoprotective effect of tetrodotoxin (TTX) alone, or in combination with a thromboxane synthetase inhibitor (OKY-046), was investigated in a 60-min warm ischemia, 72-h reperfusion, IRI rodent model.Unilateral nephrectomized rats were treated with the test vehicle alone, 1, 2, or 4 μg/kg of TTX or 2 mg/kg of OKY-046 i.v., either 15 min pre- or postischemia, or 2 μg/kg TTX administered simultaneously with OKY-046 (2 mg/kg), following the ischemic interval. Baseline, 24, and 72 h mean plasma creatinine (Cr) and urea nitrogen (BUN) were compared.Maximal renoprotection was demonstrated by significantly improved 72-h Cr and BUN levels with the 2 μg/kg of TTX or with 2 mg/kg of OKY-046, each administered after ischemia (ischemic control Cr = 8.01 ± 1.07 mg/dL vs TTX = 3.84 ± 0.80 mg/dL, P = 0.008; vs OKY-046 = 4.0 ± 1.5, P + 0.008; ischemic control BUN = 241.3 mg/dL ± 32.8 vs TTX = 85.7 mg/dL ± 18.7, P < 0.008; vs OKY-046 = 52.6 ± 22.5, P = 0.008). The combination therapy utilizing TTX with OKY-046 resulted in reduced animal survival, demonstrating no renoprotection as measured with the biochem. parameters.These results support the renoprotective effects of TTX in a severe, rodent IRI model. The exact mechanism of action, as well as the therapeutic potential of TTX in preservation/transplantation, warrants further study. (c) 1999 Academic Press.

IT 4368-28-9, Tetrodotoxin
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(effects of tetrodotoxin and OKY-046 in renal ischemia reperfusion)

RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L8 ANSWER 68 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)



REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 69 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:130120 HCAPLUS
DOCUMENT NUMBER: 130:347278
TITLE: Vanilloid receptor agonists potentiate the in vivo local anesthetic activity of percutaneously injected site 1 sodium channel blockers
AUTHOR(S): Kohane, Daniel S.; Kuang, Yu; Lu, Nu T.; Langer, Robert; Strichartz, Gary R.; Berde, Charles B.
CORPORATE SOURCE: Department of Anesthesia, Children's Hospital, Boston, MA, USA
SOURCE: Anesthesiology (1999), 90(2), 524-534
CODEN: ANESAV; ISSN: 0003-3022
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

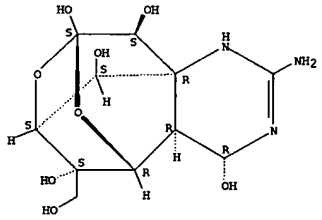
AB Background: Capsaicin, the pungent ingredient in chili peppers, is a vanilloid with noxious and analgesic effects that inhibits tetrodotoxin-resistant sodium currents. Because tetrodotoxin-resistant currents are found primarily in small-diameter nociceptor afferents of the peripheral nerves, their inhibition may lead to selective analgesia. Therefore, the authors evaluated the interactions between tetrodotoxin, a site 1 sodium channel blocker, and capsaicin on nerve blockade in vivo. Methods: Percutaneous sciatic nerve injections with 0 to 9.9 mM capsaicin, 0 to 120 μM tetrodotoxin, or both were administered to male Sprague-Dawley rats. Thermal nociceptive and motor blockade were measured. Data were expressed as medians with 25th and 75th percentiles. Results: Capsaicin produced a transient increase in thermal latency with no effect on motor strength. Tetrodotoxin reduced motor strength for a longer duration than nociception. The interaction between tetrodotoxin and capsaicin was synergistic, as evidenced by (1) supraadditive prolongation of both nociceptive and motor block, with the effect of capsaicin reversed by the vanilloid antagonist capsazepine, and (2) synergism in the frequency that rats achieved maximal block shown by isobolog. anal. The combination of tetrodotoxin and capsaicin showed less motor predominance than tetrodotoxin did alone. Similar interactions were found between tetrodotoxin and resiniferatoxin (another vanilloid), and between capsaicin and saxitoxin (another site 1 sodium channel blocker), but much less so between bupivacaine and capsaicin. Conclusions: Site 1 sodium channel blockers and vanilloids have synergistic effects on nerve blockade in vivo. These interactions may be useful in developing prolonged local anesthetics and elucidating mechanisms of functionally selective nerve blockade.

IT 4368-28-9, Tetrodotoxin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(vanilloid receptor agonists potentiate local anesthetic activity of percutaneously injected site 1 sodium channel blockers)

RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L8 ANSWER 69 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)



REFERENCE COUNT: 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 70 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:81580 HCAPLUS
DOCUMENT NUMBER: 130:148705
TITLE: Use of neurotoxin therapy for treatment of neurological-urological conditions and related disorders
INVENTOR(S): Schmidt, Richard A.; Kaula, Norbert F.
PATENT ASSIGNEE(S): University Technology Corporation, USA
SOURCE: PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9903483	A1	19990128	WO 1998-US14625	19980715
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2296720	AA	19990128	CA 1998-2296720	19980715
CA 2505930	AA	19990128	CA 1998-2505930	19980715
CA 2505933	AA	19990128	CA 1998-2505933	19980715
CA 2521392	AA	19990128	CA 1998-2521392	19980715
AU 9883007	A1	19990210	AU 1998-83007	19980715
AU 743085	B2	20020117		
EP 1011695	A1	20000628	EP 1998-933345	19980715
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001510163	T2	20010731	JP 2000-502781	19980715
JP 3692033	B2	20050907		
CN 1135986	B	20040128	CN 1998-809129	19980715
CN 1480212	A	20040310	CN 2003-2003110471	19980715
EP 1475099	A1	20041110	EP 2004-19371	19980715
EP 1475099	B1	20051228		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
EP 1502601	A1	20050202	EP 2004-26167	19980715
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
AT 314085	E	20060115	AT 2004-19371	19980715
US 6365164	B1	20020402	US 2000-463040	20000117
US 2002025327	A1	20020228	US 2001-978982	20011015
US 6667041	B2	20031223		
US 2004180065	A1	20040916	US 2003-655889	20030904
US 2004126380	A1	20040701	US 2003-685995	20031014
US 7001602	B2	20060221		
US 2004259788	A1	20041223	US 2003-745332	20031222
US 2005048084	A1	20050303	US 2004-778924	20040213
US 2005049175	A1	20050303	US 2004-778948	20040213
JP 2005089478	A2	20050407	JP 2004-367500	20041220

L8 ANSWER 70 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)

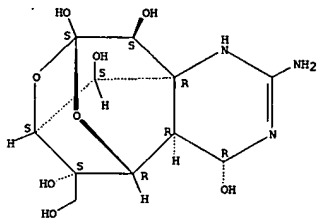
JP 2005089479	A2	20050407	JP 2004-367501	20041220
US 2005159337	A1	20050721	US 2005-77895	20050311

PRIORITY APPLN. INFO.:

US 1997-52580P	P	19970715
CA 1998-2296720	A3	19980715
EP 1998-933345	A3	19980715
JP 2000-502781	A3	19980715
WO 1998-US14625	W	19980715
US 2000-463040	A1	20000117
US 2001-978982	A2	20011015
US 2003-685995	A2	20031014

AB Methods are provided for treating neurol.-urol. conditions. This is accomplished by administration of at least one neurotoxin.
IT **4368-28-9**, Tetrodotoxin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(neurotoxins for treatment of neurol.-urol. conditions and related disorders)
RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 71 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:761807 HCAPLUS
DOCUMENT NUMBER: 130:17253
TITLE: Local anesthetic formulations
INVENTOR(S): Kohane, Daniel S.; Berde, Charles B.; Strichartz, Gary R.; Langer, Robert S.
PATENT ASSIGNEE(S): Children's Medical Center Corporation, USA; Brigham and Women's Hospital, Inc.
SOURCE: PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9851290	A2	19981119	WO 1998-US9991	19980515
WO 9851290	A3	19990211		
W: AU, CA, JP				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9873890	A1	19981208	AU 1998-73890	19980515
US 6326020	B1	20011204	US 1998-79622	19980515

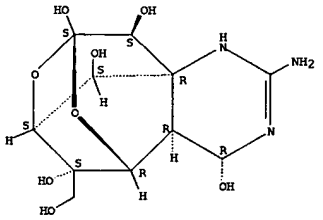
PRIORITY APPLN. INFO.:

US 1997-46163P	P	19970516
US 1997-46683P	P	19970516
US 1997-46761P	P	19970516
US 1997-53462P	P	19970723
WO 1998-US9991	W	19980515

AB Combinations of naturally occurring site 1 sodium channel blockers, such as tetrodotoxin (TTX), saxitoxin (STX), decarbamoyl saxitoxin, and neosaxitoxin (referred to jointly herein as "toxins"), with other agents, have been developed to give long duration block with improved features, including safety and specificity. The duration of the block is greatly prolonged by combining a toxin with a local anesthetic, vasoconstrictor, glucocorticoid, and/or adrenergic drugs, both α-agonists (epinephrine, phenylephrine), β-blockers (propranolol), and mixed central-peripheral α-2 agonists (clonidine), or other agents. In another embodiment, the duration of nerve block from toxin can be greatly enhanced by the inclusion of amphiphilic or lipophilic solvents. The effectiveness of these compns. is enhanced by microencapsulation within polymeric carriers, preferably biodegradable synthetic polymeric carriers. Modality specific nerve block can be obtained using combinations of toxin with vanilloids. TTX (0.2%) was combined with 50% bupivacaine and 0.05% dexamethasone in poly(glycolic acid-lactic acid) (65:35) microspheres. The carrier fluid contained 1:100.000 epinephrine to reduce toxicity. The average duration of the effective block was 7 days.
IT **4368-28-9**, Tetrodotoxin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(local anesthetic formulations)
RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L8 ANSWER 71 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)



L8 ANSWER 72 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:705872 HCAPLUS
DOCUMENT NUMBER: 130:105205
TITLE: Tetrodotoxin: anesthetic activity in the de-epithelialized cornea
AUTHOR(S): Schwartz, Daniel M.; Duncan, Keith G.; Fields, Howard L.; Jones, Matthew R.
CORPORATE SOURCE: Department of Ophthalmology, UCSF, San Francisco, CA, 94143, USA
SOURCE: Graefe's Archive for Clinical and Experimental Ophthalmology (1998), 236(10), 790-794
CODEN: GACODL; ISSN: 0721-832X
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English

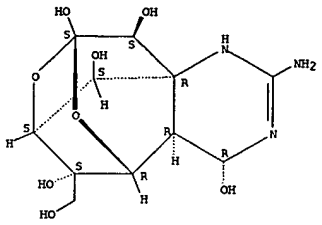
AB Background: Tetrodotoxin (TTX) binds with high affinity to sodium channels and produces local anesthesia. We investigated whether TTX is an effective, long-acting corneal anesthetic in rabbits. Methods: After mech. debridement of the central corneal epithelium, topical TTX (1 mM, 0.1 mM, or 0.01 mM) was applied to one eye each of 18 New Zealand White rabbits. The fellow eye of each rabbit was treated with control vehicle. Blink response to a mech. stimulus was assessed. Blink response was also assessed every 3 h for 30 h in 6 rabbits treated with 1 mM TTX administered every 6 h. In a sep. group of 12 rabbits with central epithelial debridement, the rate of epithelial healing was compared between animals treated with topical 1.0 mM TTX and animals receiving no treatment. Results: After 4 h, eyes treated with 1.0 mM and 0.1 mM TTX were anesthetic. At 6 h, five of six rabbit eyes treated with 1.0 mM TTX were still partially anesthetic. By 8 h, the mean anesthesia score for 1.0 mM TTX was approaching normal. With multiple dosing, all six rabbit eyes remained anesthetic for the duration of the experiment. There was no significant difference in the rate of re-epithelialization between eyes treated with TTX and untreated controls. There was no evidence of systemic or local toxicity from topical TTX. Conclusion: In a rabbit model, TTX is a long-acting topical anesthetic that retains its effectiveness when administered repeatedly over 24 h and does not inhibit epithelial healing. It may have application in management of pain after photorefractive keratectomy.

IT **4368-28-9**, Tetrodotoxin
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(tetrodotoxin anesthetic activity in the de-epithelialized cornea)

RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L8 ANSWER 72 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)



REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 73 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:682103 HCAPLUS
DOCUMENT NUMBER: 129:286010
TITLE: Method of anesthesia using a long-acting sodium channel blocker
INVENTOR(S): Schwartz, Daniel M.; Fields, Howard L.
PATENT ASSIGNEE(S): The Regents of the University of California, USA
SOURCE: PCT Int. Appl., 51 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9843619	A2	19981008	WO 1998-US6705	19980402
WO 9843619	A3	19981230		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9868837	A1	19981022	AU 1998-68837	19980402
US 6030974	A	20000229	US 1998-54800	19980402
PRIORITY APPLN. INFO.:			US 1997-40903P P	19970402
			US 1998-76317P P	19980227
			WO 1998-US6705 W	19980402

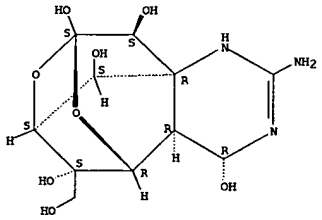
AB A method of producing local anesthesia in a mammal experiencing pain in an epithelial tissue region is described. The method includes topically administering to the region, in a suitable pharmaceutical vehicle, an ED of a long-acting sodium channel blocking compound, e.g. tetrodotoxin or saxitoxin.

IT **4368-28-9**, Tetrodotoxin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(long-acting sodium channel blocker for local anesthesia)

RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L8 ANSWER 73 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)



L8 ANSWER 74 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:541187 HCAPLUS
DOCUMENT NUMBER: 129:211637
TITLE: Mechanism of relaxant effect of clonidine in isolated bovine tracheal smooth muscle
AUTHOR(S): Arimitsu, Masashi; Mitsui-Saito, Minori; Sato, Koichi; Ozaki, Hiroshi; Koga, Yoshihisa; Karaki, Hideaki
CORPORATE SOURCE: Department of Anesthesiology, Kinki University School of Medicine, Osaka, Japan
SOURCE: Journal of Pharmacology and Experimental Therapeutics (1998), 286(2), 681-687
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

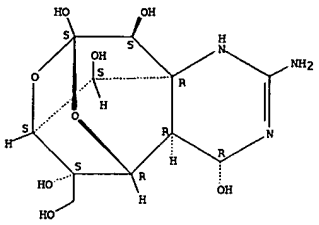
AB The relaxant effect of clonidine and the possible involvement of imidazoline I1 receptors in bovine tracheal smooth muscle (BTSM) were examined Clonidine caused concentration-dependent significant relaxation in BTSM precontracted with 0.1 or 1 μM carbachol (CCh) but not in 72.7 mM KCl-induced contraction. The relaxation in CCh-contracted BTSM was inhibited by yohimbine (1 μM) and idazoxan (10 and 30 μM) but not by tetrodotoxin, indomethacin and other adrenoceptor antagonists. Oxymetazoline (0.1-100 μM) and phentolamine (0.1-100 μM) caused concentration-dependent relaxation, which was attenuated by idazoxan (10 μM). Norepinephrine (0.1-100 μM) produced concentration-dependent relaxation, which was completely abolished by propranolol (10 μM) but not by yohimbine (1 μM). In fura-PE3/AM-loaded BTSM, CCh and 72.7 mM KCl increased intracellular calcium concentration ([Ca++]i) followed by contraction. The high K+-induced increase in [Ca++]i was not affected by clonidine. In CCh-stimulated BTSM, clonidine decreased [Ca++]i and muscle force in parallel, whereas verapamil decreased [Ca++]i more strongly than muscle force. Clonidine (100 μM) inhibited the transient increase in [Ca++]i induced by CCh but not by caffeine (20 mM) in Ca++-free solution Clonidine did not change the cAMP content in the presence of either 72.7 mM KCl or CCh. These results indicate that clonidine relaxes CCh-stimulated BTSM through the inhibition of CCh-induced increases in Ca++-influx, Ca++-release and intracellular signal transduction probably via imidazoline I1 receptors.

IT **4368-28-9**, Tetrodotoxin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mechanism of relaxant effect of clonidine in isolated bovine tracheal smooth muscle)

RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L8 ANSWER 74 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)



REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 75 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:477704 HCAPLUS
DOCUMENT NUMBER: 129:239784
TITLE: A re-examination of tetrodotoxin for prolonged duration local anesthesia
AUTHOR(S): Kohane, Daniel S.; Yieh, Jamie; Lu, Nu T.; Langer, Robert; Strichartz, Gary R.; Berde, Charles B.
CORPORATE SOURCE: Harvard Medical School, Massachusetts General Hospital, Children's Hospital, Brigham and Women's Hospital, Boston, MA, 02115, USA
SOURCE: Anesthesiology (1998), 89(1), 119-131
CODEN: ANESAV; ISSN: 0003-3022
PUBLISHER: Lippincott-Raven Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English

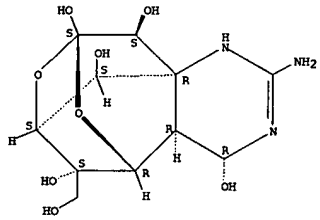
AB Highly potent toxins such as tetrodotoxin that block sodium channels with great specificity have been studied for many years and can provide prolonged blockade when coadministered with vasoconstrictors or conventional local anesthetics. Their utility has been constrained, however, by systemic toxicity. The authors examined the efficacy of tetrodotoxin with and without epinephrine or bupivacaine for producing prolonged-duration sciatic nerve blockade in the rat, and they assessed the degree of concomitant toxicity. Rats received percutaneous sciatic nerve blockade using tetrodotoxin with and without epinephrine or bupivacaine. A subset received s.c. injections at the nuchal midline. Nociceptive, proprioceptive, and motor blockade were quantified using contralateral leg responses as controls for systemic effects. Tetrodotoxin without epinephrine produced sciatic nerve blockade, but with considerable toxicity at most EDs. Epinephrine reduced the median effective concentration of tetrodotoxin for nociception from 37.6 to 11.5 μM and prolonged its duration, such that reversible blocks lasting >13 h were achieved. Epinephrine reduced measures of systemic distribution and increased the median LD of tetrodotoxin from 40 to 53.6 nmole/kg, thus more than quadrupling the therapeutic index. Bupivacaine increased the local anesthetic potency of tetrodotoxin, reduced its systemic toxicity, and, when coinjected s.c., increased the median LD from 43.7 to 47.7 nmole/kg. The addition of epinephrine did not further improve the effectiveness of the bupivacaine-tetrodotoxin combination. Combinations of epinephrine or bupivacaine with tetrodotoxin or with other high-potency toxins active on sodium channels should be examined for the potential to provide clin. useful, prolonged nerve blockade.

IT **4368-28-9**, Tetrodotoxin
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bupivacaine or epinephrine interaction with tetrodotoxin for prolonged duration local anesthesia)

RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L8 ANSWER 75 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)



REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

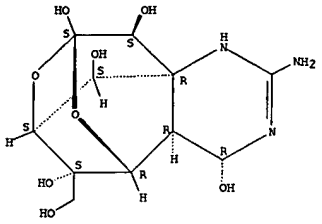
L8 ANSWER 76 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:339592 HCAPLUS
DOCUMENT NUMBER: 129:62683
TITLE: Protection against myocardial ischemic/reperfusion injury by inhibitors of two separate pathways of Na+ entry
AUTHOR(S): Eng, Stanley; Maddaford, Thane G.; Kardami, Elissavet; Pierce, Grant N.
CORPORATE SOURCE: Division of Stroke and Vascular Diseases, Inst. of Cardiovascular Sciences, St. Boniface General Hospital Res. Centre, Winnipeg, MB, Can.
SOURCE: Journal of Molecular and Cellular Cardiology (1998), 30(4), 829-835
CODEN: JMCDAY; ISSN: 0022-2828
PUBLISHER: Academic Press Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Previous work has demonstrated that drugs in combination will have an additive protective effect in Langendorff-perfused hearts. During reperfusion following 30 min of ischemia, developed tension and resting tension were 34±3 and 162±5%, resp., of pre-ischemic values in non-treated ischemic hearts. The administration of HOE-642 to inhibit Na+/H+ exchange increased active developed tension (DT) to 58±2% of pre-ischemic levels and decreased resting tension (RT) to 111±3% of pre-ischemic levels. The administration of tetrodotoxin (TTX) to block the Na+ channel increased DT to 56±3% of the pre-ischemic level and reduced the Rt to 1.26±12% of the pre-ischemic level. Together, HOE-642 and TTX increased recovery of DT to 63±2% of pre-ischemic levels and improved RT to 116±4% of pre-ischemic levels after 30 min of reperfusion. All drug treatment protocols significantly lowered the creatine phosphokinase activity measured in the coronary effluent in comparison to that observed in the non-treated hearts. These data demonstrate that inhibition of Na+ entry through either Na+-H+ exchange or the Na+ channel protects the heart from ischemic injury, but there is no addnl. benefit of blocking both routes of Na+ entry simultaneously. This suggests that a threshold level of Nai+ may be a critical factor in ischemic cardioprotection.

IT **4368-28-9**, Tetrodotoxin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(protection against myocardial ischemic/reperfusion injury by inhibitors of two sep. pathways of Na+ entry)
RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L8 ANSWER 76 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)



REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

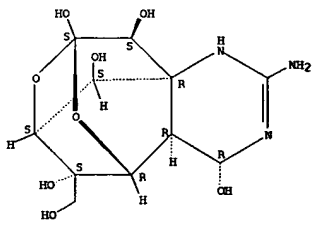
L8 ANSWER 77 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:119609 HCAPLUS
DOCUMENT NUMBER: 128:132452
TITLE: Compositions containing tetrodotoxin for use as analgesics and in termination of drugs of abuse
INVENTOR(S): Wang, Weiguo
PATENT ASSIGNEE(S): Wang, Weiguo, Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 7 pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1145225	A	19970319	CN 1996-119454	19960924
CN 1072486	B	20011010		
PRIORITY APPLN. INFO.:			CN 1996-119454	19960924

AB Compns. containing tetrodotoxin and their use as analgesics and for termination of drugs of abuse are claimed. An injection for pain in cancer patients at the terminal stage contained tetrodotoxin [0.5-10.0 μg/ 1-20 mL] and acetic acid [pH 4-5].

IT **4368-28-9**, Tetrodotoxin
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(compns. containing tetrodotoxin for use as analgesics and in termination of drugs of abuse)
RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L8 ANSWER 78 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1997:640562 HCAPLUS
DOCUMENT NUMBER: 127:298748
TITLE: Injectable therapy with botulinum toxin for control of muscle spasms and pain related to muscle spasms
INVENTOR(S): Aoki, Kei Roger; Wheeler, Larry A.; Garst, Michael E.
PATENT ASSIGNEE(S): Allergan, USA
SOURCE: PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

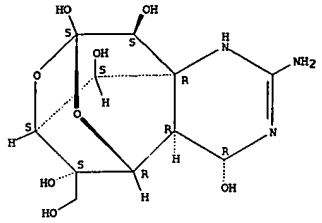
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9734624	A1	19970925	WO 1997-US4643	19970320
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5721215	A	19980224	US 1996-619780	19960320
CA 2249196	AA	19970925	CA 1997-2249196	19970320
AU 9723417	A1	19971010	AU 1997-23417	19970320
AU 716374	B2	20000224		
EP 889731	A1	19990113	EP 1997-916168	19970320
EP 889731	B1	20041124		
R: DE, ES, FR, GB, IT				
JP 2000508629	T2	20000711	JP 1997-533754	19970320
ES 2232864	T3	20050601	ES 1997-916168	19970320
PRIORITY APPLN. INFO.:			US 1996-619780 A	19960320
			WO 1997-US4643 W	19970320

AB A method for administration of botulinum toxin, includes the steps of (a) selecting at least one neuromuscular blocking agent having a duration of activity shorter than neuromuscular blocking activity of botulinum toxin; (b) selecting at least one muscle of a muscle group; (c) i.m. injecting the selected agent into the selected muscle; (d) observing muscle relaxation in both the selected muscle and other non-selected muscles in the muscle group to determine spill-over, muscle tone and balance; (e) repeating steps (b) - (d) until a final muscle selection is found; and (f) i.m. injecting botulinum toxin into the final muscle selection.

IT **4368-28-9**, Tetrodotoxin
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(injectable therapy with botulinum toxin for control of muscle spasms and pain related to muscle spasms)
RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L8 ANSWER 78 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)



L8 ANSWER 79 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1997:573035 HCAPLUS
DOCUMENT NUMBER: 127:243149
TITLE: Sodium channel modulators prevent oxygen and glucose deprivation injury and glutamate release in rat neocortical cultures
AUTHOR(S): Probert, A. W.; Borosky, S.; Marcoux, F. W.; Taylor, C. P.
CORPORATE SOURCE: Parke-Davis Research Division, Department of Neurological and Neurodegenerative Diseases, Warner-Lambert Company, Ann Arbor, MI, 48105, USA
SOURCE: Neuropharmacology (1997), 36(8), 1031-1038
CODEN: NEPHBW; ISSN: 0028-3908
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

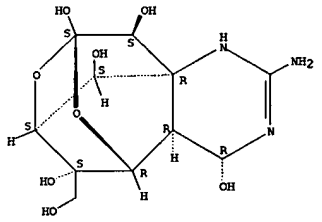
AB Neocortical cultures were deprived of oxygen and glucose to model ischemic neuronal injury. The authors used a graded series of periods of oxygen and glucose deprivation, providing graded insults. Cell death was measured by release of lactate dehydrogenase (LDH). One hundred and twenty to 240 min of deprivation caused graded increases in glutamate overflow, LDH release and 45Ca influx. Curves of LDH release with respect to deprivation time were shifted to longer intervals by treatment with tetrodotoxin (TTX; 3, 30 or 300 nM), phenytoin (10, 30 or 100 μM), lidocaine (10, 30 or 100 μM) or the N-methyl-D-aspartate antagonist CPP [3(2-carboxypiperazine-4-yl)propyl-1-phosphonic acid, 3, 10, 30 or 100 μM]. Combined treatment with TTX and CPP caused pronounced rightward shifts of LDH deprivation curves. The results indicate that Na+ channel blockade is neuroprotective in neocortex cultures. The results also suggest that neuroprotection with Na+ channel blockers may be due to inhibition of glutamate release.

IT **4368-28-9**, Tetrodotoxin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(sodium channel modulators prevent oxygen and glucose deprivation injury and glutamate release in rat neocortical cultures as model of ischemic neuronal injury)

RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L8 ANSWER 79 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)



REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 80 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1997:407334 HCAPLUS
DOCUMENT NUMBER: 127:104106
TITLE: Beneficial effects of dilazep on the palmitoyl-L-carnitine-induced derangements in isolated, perfused rat heart: comparison with tetrodotoxin
AUTHOR(S): Hara, Akiyoshi; Arakawa, Johji; Hashizume, Hiroko; Abiko, Yasushi
CORPORATE SOURCE: Department of Pharmacology, Asahikawa Medical College, Asahikawa, 078, Japan
SOURCE: Japanese Journal of Pharmacology (1997), 74(2), 147-153
CODEN: JJPAAZ; ISSN: 0021-5198
PUBLISHER: Japanese Pharmacological Society
DOCUMENT TYPE: Journal
LANGUAGE: English

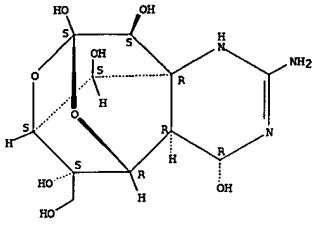
AB The present study was carried out to determine the effect of dilazep, having an inhibitory effect on the Na+ channel, on the mech. dysfunction and metabolic derangements induced by palmitoyl-L-carnitine in isolated rat heat and to compare the effect of dilazep with that of tetrodotoxin, a specific inhibitor of the Na+ channel. Rat heart were perfused aerobically at a constant flow according to Langendorff's technique and paced elec. Palmitoyl-L-carnitine (5 μM) decreased the left ventricular developed pressure and increased the left ventricular end diastolic pressure (i.e., it produced mech. dysfunction), decreased the tissue level of ATP and increased the tissue level of adenosine monophosphate (i.e., it produced metabolic derangements). These mech. and metabolic alterations induced by palmitoyl-L-carnitine were attenuated by either dilazep (1 μM) or tetrodotoxin (3 μM). Neither dilazep nor tetrodotoxin modified the mech. function and energy metabolism of the normal (palmitoyl-L-carnitine-untreated) heart. These results suggest that inhibition of the Na+ channel with dilazep or tetrodotoxin is responsible, at least in part, for attenuating the palmitoyl-L-carnitine-induced mech. dysfunction and metabolic derangements in the heart.

IT **4368-28-9**, Tetrodotoxin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(beneficial effects of dilazep on palmitoyl-L-carnitine-induced derangements in isolated perfused rat heart and comparison with tetrodotoxin in relation to sodium channel blockade and energy metabolism)

RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

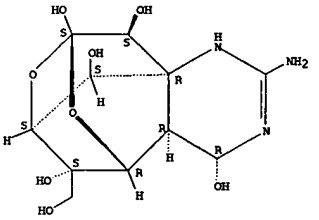
L8 ANSWER 80 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)



L8 ANSWER 81 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)

CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L8 ANSWER 81 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1997:199533 HCAPLUS
DOCUMENT NUMBER: 126:287924
TITLE: The protective action of tetrodotoxin and (±)-kavain on anaerobic glycolysis, ATP content and intracellular Na+ and Ca2+ of anoxic brain vesicles
AUTHOR(S): Gleitz, Johannes; Tosch, Claudia; Beile, Anne; Peters, Thies
CORPORATE SOURCE: University Clinics Ulm, Institute of Naturheilkunde, Ulm, 89081, Germany
SOURCE: Neuropharmacology (1997), Volume Date 1996, 35(12), 1743-1752
CODEN: NEPHBW; ISSN: 0028-3908
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Because recent reports point to Na+ channel blockers as protective agents directed against anoxia-induced neuronal damage including protection of anaerobic glycolysis, the influences of tetrodotoxin (TTX) and (±)-kavain on anoxic rat brain vesicles were investigated with respect to lactate synthesis, vesicular ATP content and cytosolic free Na+ and Ca2+ [Na+]i, [Ca2+]i, both of the latter determined fluorometrically employing SBFI and FURA-2, resp. After anoxia, basal lactate production was increased from 2.9 to 9.8 nmol lactate/min/mg protein. Although lactate synthesis seemed to be stable for at least 45 min of anoxia, as deduced from the linearity of lactate production, the ATP content declined continuously with a half life (τ1/2) of 14.5 min, indicating that anaerobic glycolysis was insufficient to cover the energy demand of anoxic vesicles. Correspondingly, [Na+]i and [Ca2+]i increased persistently after anoxia by 22.1 nM Na+ and 274.9 nM Ca2+, determined 6.3 min after onset. An addnl. stimulation of vesicles with veratridine accelerated the drop of ATP (τ1/2 = 5.1 min) and provoked a massive Na+ overload, which leveled off to 119 mM Na+ within a few minutes. Concomitantly, [Ca2+]i increased linearly with a rate of 355 nmol Ca2+/L/min. Despite the massive perturbation of ion homeostasis, lactate production was unaffected during the first 8 min of veratridine stimulation. However, complete inhibition of lactate synthesis took place 30 min after veratridine was added. The Na+ channel blockers TTX and (±)-kavain, if applied before anoxia, preserved vesicular ATP content, diminished anoxia-induced increases in [Na+]i and [Ca2+]i and prevented both the veratridine-induced increases of [Na+]i and [Ca2+]i and the inhibition of lactate production The data indicate a considerable Na+ influx via voltage-dependent Na+ channels during anoxia, which speeds up the decline in ATP and provokes an increase in [Ca2+]i. A massive Na+ and Ca2+ overload induced by veratridine failed to influence lactate synthesis directly, but initiated its inhibition.

IT **4368-28-9**, Tetrodotoxin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(protective action of tetrodotoxin and kavain on anaerobic glycolysis and ATP content and intracellular Na+ and Ca2+ of anoxic brain vesicles)

RN 4368-28-9 HCAPLUS

L8 ANSWER 82 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN

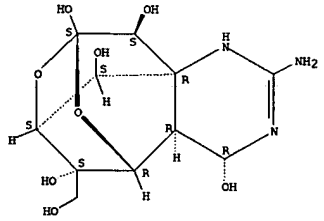
ACCESSION NUMBER: 1997:87693 HCAPLUS
DOCUMENT NUMBER: 126:126698
TITLE: Effects of antiarrhythmic agents and Mg2+ on aconitine-induced arrhythmias
AUTHOR(S): Sawanobori, Tohru; Adaniya, Hitoshi; Hirano, Yuji; Hiraoka, Masayasu
CORPORATE SOURCE: Department of Cardiovascular Diseases, Medical Research Institute, Tokyo Medical and Dental University, Tokyo, Japan
SOURCE: Japanese Heart Journal (1996), 37(5), 709-718
CODEN: JHEJAR; ISSN: 0021-4868
PUBLISHER: Japanese Heart Journal Association
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The effects of antiarrhythmic agents, including Class I and IV drugs and 3-10 mM Mg2+, on aconitine-induced arrhythmias were examined by using a conventional microelectrode and patch-clamp method in Langendorff-perfused rabbit hearts and isolated guinea pig ventricular myocytes. Intracoronary administration of 0.1 μM aconitine induced polymorphic ventricular tachycardia (PVT) which continued for >60 min. Addition of aconitine to ventricular myocytes caused a prolonged action potential duration (APD) and the appearance of early after-depolarization (EAD), together with the occurrence of an inward hump of the I-V curve around -60 to -40 mV and increased outward current at pos. voltages. Addition of 10 μM tetrodotoxin (TTX) and ≥5 mM Mg2+ restored aconitine-induced PVT to sinus rhythm in Langendorff-perfused prepns. and also shortened the prolonged APD, demonstrating the abolition of EAD by aconitine in ventricular myocytes. However, antiarrhythmic agents did not exert such effects. In conclusion, the antiarrhythmic actions of Mg2+ and TTX in aconitine-induced arrhythmia are to abolish EAD and shorten the prolonged APD by suppression of the inward Na+ current around -60 to -40 mV.

IT **4368-28-9**, Tetrodotoxin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(aconitine-induced heart arrhythmias response to)

RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

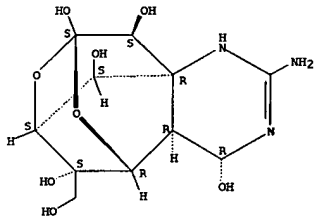


L8 ANSWER 82 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)
REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 83 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1997:16863 HCAPLUS
DOCUMENT NUMBER: 126:207394
TITLE: Altered Na+-channel function as an in vitro model of the ischemic penumbra: action of lubeluzole and other neuroprotective drugs
AUTHOR(S): Ashton, David; Willems, Roland; Wynants, Jozef; Van Reempts, Jos; Marrannes, Roger; Clincke, Gilbert
CORPORATE SOURCE: Department of Neuropsychopharmacology, Janssen Research Foundation, Turnhoutseweg 30, Beerse, 2340, Belg.
SOURCE: Brain Research (1997), 745(1,2), 210-221
CODEN: BRREAP; ISSN: 0006-8993
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Veratridine blocks Na+-channel inactivation and causes a persistent Na+-influx. Exposure of hippocampal slices to 10 μM veratridine led to a failure of synaptic transmission, repetitive spreading depression (SD)-like depolarizations of increasing duration, loss of Ca+-homeostasis, a large reduction of membrane potential, spongious edema and metabolic failure. Normalization of the amplitude of the neg. DC shift evoked by high K+ ACSF 80 min after veratridine exposure was taken as the primary endpoint for neuroprotection. Compds. whose mechanism of action includes Na+-channel modulation were neuroprotective (IC50-values in μM): tetrodotoxin 0.017, verapamil 1.18, riluzole 1.95, lamotrigine ≥10, and diphenylhydantoin 16.1. Both NMDA (MK-801 and APH) and non-NMDA (NBQX) excitatory amino acid antagonists were inactive, as were NOS-synthesis inhibitors (nitro-L-arginine and L-NAME), Ca2+-channel blockers (cadmium, nimodipine), and a K+-channel blocker (TEA). Lubeluzole significantly delayed the time before the slices became epileptic, postponed the first SD-like depolarization, allowed the slices to better recover their membrane potential after a larger number of SD-like DC depolarizations, preserved Ca2+ and energy homeostasis, and prevented the neurotoxic effects of veratridine (IC50-value 0.54 μM). A concentration of lubeluzole, which was 40+ higher than its IC50-value for neuroprotection against veratridine, had no effect on repetitive Na+-dependent action potentials induced by depolarizing current in normal ACSF. The ability of lubeluzole to prevent the pathol. consequences of excessive Na+-influx, without altering normal Na+-channel function may be of benefit in stroke.
IT **4368-28-9**, Tetrodotoxin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(altered Na+-channel function as in vitro model of ischemic penumbra in hippocampus and action of lubeluzole and other neuroprotective drugs)
RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

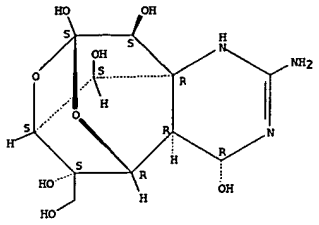
L8 ANSWER 83 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)



L8 ANSWER 84 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1996:347149 HCAPLUS
DOCUMENT NUMBER: 125:48803
TITLE: Prevention of reoxygenation-induced arrhythmias in guinea pig papillary muscles
AUTHOR(S): Hayashi, Hideharu; Terada, Hajime; Katoh, Hideki; McDonald, T. F.
CORPORATE SOURCE: Photon Med. Res. Cent., Hamamatsu Univ. Sch. Med., Hamamatsu, 431-31, Japan
SOURCE: Journal of Cardiovascular Pharmacology (1996), 27(6), 816-823
CODEN: JCPCDT; ISSN: 0160-2446
PUBLISHER: Lippincott-Raven
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Effects of various agents on reoxygenation-induced arrhythmias, action potentials, and tension of guinea pig papillary muscles were recorded to investigate the site of action. Triggered activities due to delayed afterdepolarizations (DADs) and aftercontractions were elicited on reoxygenation after 60-min substrate-free hypoxia. Low extracellular Ca2+ (0.1 mM) abolished arrhythmias, and high Ca2+ (4.9 mM) increased the amplitudes of DADs and aftercontractions. D-600 at a high concentration (20 μM) decreased the incidence of arrhythmias and decreased the recovery of developed tension after reoxygenation. Ryanodine (1 μM) abolished aftercontractions and arrhythmias but did not affect the recovery of developed tension. Tetrodotoxin (TTX 3 μM) and nicorandil (100 μM) decreased the incidence of arrhythmias, but did not affect the recovery of developed tension or the amplitudes of aftercontractions. TTX caused only a slight decrease in Ca2+ transients in a fluo-3-loaded guinea pig ventricular myocyte. The Ca2+ entry through the Ca2+ channels apparently synchronized Ca2+ release from the sarcoplasmic reticulum, and D-600 at the high concentration apparently decreased the incidence of arrhythmias. TTX and nicorandil decreased arrhythmias, probably by decreasing the Na+ current or by increasing the ATP-sensitive K+ current, resp.
IT **4368-28-9**, Tetrodotoxin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(prevention of reoxygenation-induced arrhythmias in guinea pig papillary muscles)
RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L8 ANSWER 84 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)



L8 ANSWER 85 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1996:93087 HCAPLUS
DOCUMENT NUMBER: 124:194121
TITLE: Selective suppression of in vitro electrographic seizures by low-dose tetrodotoxin: A novel anticonvulsant effect
AUTHOR(S): Burack, Michelle A.; Stasheff, Steven F.; Wilson, Wilkie A.
CORPORATE SOURCE: Medical Center, Duke University, Durham, NC, 27710, USA
SOURCE: Epilepsy Research (1995), 22(2), 115-26
CODEN: EPIRE8; ISSN: 0920-1211
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

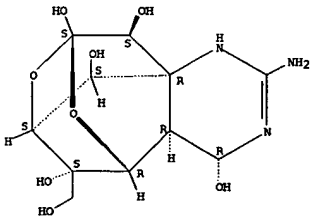
AB Localized injections of 50 μM tetrodotoxin (TTX) in rat hippocampal slices blocked stimulus train-evoked electrog. seizures (EGSs) for several hours. Responses to single stimuli were minimally altered during TTX block of the EGSs. This selective reduction of epileptiform activity could result from general blockade of action potentials in an anatomically distinct group of neurons in the slice. To test this hypothesis, we systematically mapped TTX injection sites in the hippocampal slice, and found that TTX injections that blocked EGSs were nearly always located in or invaded CA2/3 stratum radiatum and/or stratum lacunosum-moleculare. A high degree of recurrent activity in this region contributes to both epileptiform activity and responses to single stimuli; hence our selective inhibition of EGSs suggests a more pharmacol. specific anticonvulsant effect of TTX. Consistent with this hypothesis, we found that low concns. of TTX (5, 10, or 20 nM) in the perfusion medium blocked EGSs without decreasing the amplitude of extracellular responses to single stimuli. Polysynaptic activity and/or antidromic firing may be particularly vulnerable to TTX action on voltage-gated sodium channels, due to their lower the safety factor for action potential propagation. Selective reduction of this activity may disrupt the abnormal neuronal activity underlying EGSs.

IT **4368-28-9**, Tetrodotoxin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(selective suppression of in vitro electrog. seizures by low-dose tetrodotoxin)

RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L8 ANSWER 85 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)



L8 ANSWER 86 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1995:967255 HCAPLUS
DOCUMENT NUMBER: 124:807
TITLE: Use of amino group-containing hydrogenated quinazoline compounds and derivatives thereof for the termination of drug dependence
INVENTOR(S): Pan, Xinfu; Qiu, Fanglong
PATENT ASSIGNEE(S): Nanning Maple Leaf Pharmaceutical Co., Ltd., Peop. Rep. China
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9524903	A1	19950921	WO 1995-CN16	19950311
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TT, UA				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9518881	A1	19951003	AU 1995-18881	19950311
EP 750909	A1	19970102	EP 1995-911187	19950311
EP 750909	B1	20021211		
R: BE, DE, FR, GB				
JP 09510221	T2	19971014	JP 1995-523758	19950311
RU 2168331	C2	20010610	RU 1996-121334	19950311
US 5846975	A	19981208	US 1996-640781	19960521
PRIORITY APPLN. INFO.:			CN 1994-110873 A	19940317
			WO 1995-CN16 W	19950311

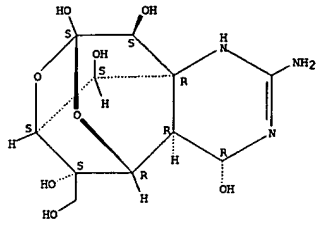
AB This invention relates to the use of amino group-containing hydrogenated quinazoline compds. and derivs. thereof, such as tetrodotoxin, for the termination of drug dependence in humans. Amino group-containing hydrogenated quinazoline compds. are administered s.c., i.m. or i.v. to subjects, and the said drugs are alkaloids and nitrogen-containing non-amino acid compds. such as opium, morphine, and heroin. The therapeutic amino group-containing hydrogenated quinazoline compds. are nonhabit-forming and fast-acting and show min. side effects.

IT **4368-28-9D**, Tetrodotoxin, derivs.
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(use of amino group-containing hydrogenated quinazoline compds. and derivs. thereof for the termination of drug dependence)

RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L8 ANSWER 86 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)



L8 ANSWER 87 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1995:765847 HCAPLUS
DOCUMENT NUMBER: 123:218028
TITLE: Alleviation of contractile dysfunction in ischemic hearts by slowly inactivating Na+ current blockers
AUTHOR(S): Le Grand, B.; Vie, B.; Talmant, J. M.; Coraboeuf, E.; John, G. W.
CORPORATE SOURCE: Div. Cardiovascular Diseases, Cent. Recherche Pierre Fabre, Castres, 81106, Fr.
SOURCE: American Journal of Physiology (1995), 269(2, Pt. 2), H533-H540
CODEN: AJPHAP; ISSN: 0002-9513
PUBLISHER: American Physiological Society
DOCUMENT TYPE: Journal
LANGUAGE: English

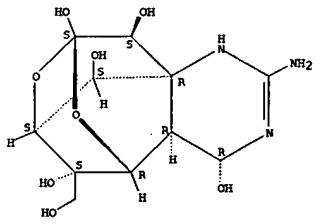
AB The authors hypothesized that the slowly inactivating component of Na+ current, which is an integral part of the Na+ window current, is a major pathway for Na+ loading during myocardial ischemia. The putative protective effects of tetrodotoxin (TTX) and R-56865, at concns. that selectively blocked the Na+ window current, as assessed by action potential plateau shortening without affecting maximum upstroke velocity (Vmax), were examined in isolated Langendorff-perfused guinea pig hearts subjected to 50 min of normothermic global ischemia and 60 min of reperfusion. In papillary muscles, TTX reduced action potential duration at ≥10 nM but reduced Vmax only at ≥1 μM. R-56865 (10 nM-10 μM) failed to affect Vmax but concentration dependently reduced action potential duration. Ischemia-induced cardiac dysfunction, including increases in left ventricular end-diastolic pressure and lactate dehydrogenase and creatine phosphokinase release at reperfusion, was attenuated by TTX and R-56865 (0.1-320 nM). Ischemic contracture (increase in left ventricular end-diastolic pressure) was abolished by drug concns. as low as 1 nM, whereas higher concns. (>10 nM) of TTX and R-56865 were required to restore systolic function at reperfusion. TTX and R-56865 had little or no effect on hemodynamic variables. Evidence is provided of pronounced and direct cardioprotective effects of low concns. of R-56865 and TTX in cardiac muscle during ischemia. The results indicate that these drugs can selectively attenuate the Na+ window current without affecting the fast peak of the Na+ current and that the slow component of Na current may constitute a pathway of early Na+ loading in the ischemic myocyte.

IT **4368-28-9**, Tetrodotoxin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(alleviation of contractile dysfunction in ischemic hearts by slowly inactivating Na+ current blockers)

RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L8 ANSWER 87 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)



L8 ANSWER 88 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1995:505711 HCAPLUS
DOCUMENT NUMBER: 122:282076
TITLE: Sodium channel blockers reduce oxygen-glucose deprivation-induced cortical neuronal injury when combined with glutamate receptor antagonists
AUTHOR(S): Lynch, James J., III; Yu, Shan P.; Canzoniero, Lorella M. T.; Sensi, Stefano L.; Choi, Dennis W.
CORPORATE SOURCE: Department Neurology, Washington School Medicine, St. Louis, MO, USA
SOURCE: Journal of Pharmacology and Experimental Therapeutics (1995), 273(1), 554-60
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

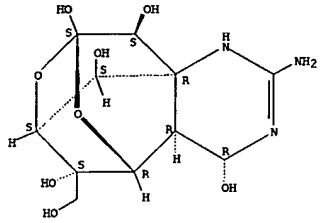
AB Blockers of voltage-gated Na+ channels can protect central neuronal axons from hypoxic injury in vitro but have shown limited neuroprotective effects on neurons, where substantial injury is mediated by glutamate receptors. The authors explored the ability of several voltage-gated Na+ channel blockers to protect murine cultured cortical neurons from injury induced by oxygen-glucose deprivation. Whole-cell recordings from neurons revealed two types of Na+ currents activated by membrane depolarization: one rapidly inactivating and the other noninactivating. Both currents were blocked by tetrodotoxin (TTX) and 5,5-diphenylhydantoin (phenytoin). Fluorescent imaging using the Na+-selective dye SBFI confirmed that TTX attenuated the increase in intracellular free Na+ induced by oxygen-glucose deprivation. Addition of TTX (1 μM) but not phenytoin (10-100 μM) produced a small and variable reduction in neuronal death subsequent to oxygen-glucose deprivation for 40 to 50 min. Blockade of glutamate neurotoxicity by combined addition of MK-801, 7-chlorokynurenate and 6-cyano-7-nitroquinoxaline-2,3-dione markedly reduced injury such that prolonged deprivation times (75-100 min) were needed to induce widespread neuronal death. In this setting of glutamate receptor blockade, addition of TTX, phenytoin or one of several other Na+ channel blockers-lidocaine (100 μM), QX-314 (1 mM), quinidine (100 μM) or lorcainide (10 or 100 μM)-all further reduced neuronal death. Present results raise the possibility that Na+ channel blockers may be useful in protecting gray matter from hypoxic-ischemic injury, especially when combined with anti-excitotoxic approaches.

IT **4368-28-9**, Tetrodotoxin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(sodium channel blockers reduce oxygen-glucose deprivation-induced cortical neuronal injury when combined with glutamate receptor antagonists)

RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L8 ANSWER 88 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)



L8 ANSWER 89 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1995:292090 HCAPLUS
DOCUMENT NUMBER: 122:71814
TITLE: Neuroprotective effects of tetrodotoxin as a Na+ channel modulator and glutamate release inhibitor in cultured rat cerebellar neurons and in gerbil global brain ischemia
AUTHOR(S): Lysko, Paul G.; Webb, Christine L.; Yue, Tian-Li; Gu, Juan-Li; Feuerstein, Giora
CORPORATE SOURCE: Cardiovascular Pharmacology, SmithKline Beecham Pharmaceuticals, King of Prussia, PA, 19406-0939, USA
SOURCE: Stroke (1994), 25(12), 2476-82
CODEN: SJCCA7; ISSN: 0039-2499
DOCUMENT TYPE: Journal
LANGUAGE: English

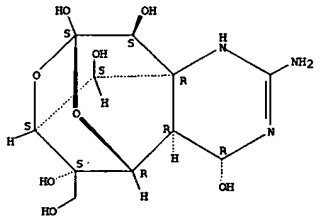
AB Studies examining the role of tetrodotoxin-sensitive ion channels in hypoxic-ischemic neuronal damage have concluded that sodium influx is an important initiating event. The authors examined the neuroprotectant effect of tetrodotoxin on both cultured cerebellar neurons and on CA1 hippocampal neurons of gerbils exposed to brain ischemia. The authors studied neuroprotective mechanisms using cultured rat cerebellar granule cells exposed to veratridine, which induced cytotoxicity, neurotransmitter release, and calcium influx. Survival of gerbil CA1 neurons was examined by direct neuron counts 7 days after 6 min of global ischemia with reperfusion. Tetrodotoxin protected cultured neurons in a dose-dependent manner from veratridine-induced toxicity (protective concentration [PC50]=22 nmol/L). Veratridine induced [3H]aspartate efflux that was sodium dependent, only 25% calcium dependent, and was inhibited by tetrodotoxin (inhibitory concentration [IC50]=60 nmol/L). Veratridine initiated increases in intracellular calcium that were also reversed by tetrodotoxin (IC50=63 nmol/L); reversal was dependent on the sodium-calcium exchanger and the sodium-potassium pump. Neuroprotection of 90% (vs. vehicle) of gerbil CA1 hippocampal neurons was achieved by pretreatment with 2 ng of tetrodotoxin delivered three times intracerebroventricularly, without causing hypothermia. Sodium channel blockers like tetrodotoxin may have utility in treatment of ischemic neuronal injury by preventing excessive neuronal depolarizations, limiting excitotoxic glutamate release through reversal of the sodium-dependent glutamate transporter, preventing intracellular calcium overload, preserving cellular energy stores, and allowing recovery of ionic homeostasis through operation of the sodium-calcium exchanger.

IT **4368-28-9**, Tetrodotoxin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(neuroprotective effects of tetrodotoxin as Na+ channel modulator and glutamate release inhibitor in cultured rat cerebellar neurons and in gerbil global brain ischemia)

RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L8 ANSWER 89 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)



L8 ANSWER 90 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN

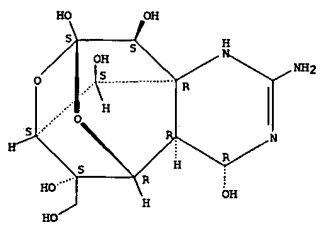
ACCESSION NUMBER: 1994:692678 HCAPLUS
DOCUMENT NUMBER: 121:292678
TITLE: Damage from oxygen and glucose deprivation in hippocampal slices is prevented by tetrodotoxin, lidocaine and phenytoin without blockade of action potentials
AUTHOR(S): Weber, Mark L.; Taylor, Charles P.
CORPORATE SOURCE: Department of Neuroscience Pharmacology, Parke-Davis Pharmaceutical Research, Division of Warner-Lambert Co., 2800 Plymouth Rd., Ann Arbor, MI, 48105, USA
SOURCE: Brain Research (1994), 664(1/2), 167-77
CODEN: BRREAP; ISSN: 0006-8993
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In vitro ischemia (IVI) was simulated with rat hippocampal slices in medium lacking D-glucose, equilibrated with 95% nitrogen, 5% carbon dioxide. Within 5-8 min, synaptic potentials disappeared and a DC neg. shift (5-15 mV) occurred. Prolonged application of 95% oxygen and D-glucose 12 min later did not allow synaptic potentials to recover. Slices pretreated with sodium channel blocking drugs allowed synaptic potentials to recover after IVI. Tetrodotoxin (TTX, 100-600 nM), the anticonvulsant phenytoin (5.0 to 100 μM) and the local anesthetic lidocaine (2.0 to 200 μM) each delayed or prevented neg. DC shifts from IVI. Histol. examination showed that drug treatments also prevented CA1 pyramidal cell damage from IVI. Neuroprotection occurred without blocking synaptic potentials or presynaptic fiber volleys, suggesting relevance for treatment of brain ischemia.

IT **4368-28-9**, Tetrodotoxin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(damage from hippocampal ischemia is prevented by tetrodotoxin and lidocaine and phenytoin without blockade of action potentials)

RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L8 ANSWER 91 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1994:646337 HCAPLUS
DOCUMENT NUMBER: 121:246337
TITLE: Methods for treating neurodegenerative diseases and disorders using N-(2,6-disubstituted aromatic)-N'-pyridinyl ureas and other anticonvulsant compounds
INVENTOR(S): Taylor, Charles Price, Jr.; Weber, Mark Lawrence
PATENT ASSIGNEE(S): Warner-Lambert Co., USA
SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 9418972	A2	19940901	WO 1994-US1788		19940217
WO 9418972	A3	19941222			
W: AU, CA, CZ, FI, HU, JP, KR, NO, NZ, RU, SK					
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
US 6133299	A	20001017	US 1993-23016		19930225
AU 9462695	A1	19940914	AU 1994-62695		19940217
PRIORITY APPLN. INFO.:			US 1993-23016	A	19930225
			WO 1994-US1788	W	19940217

OTHER SOURCE(S): MARPAT 121:246337

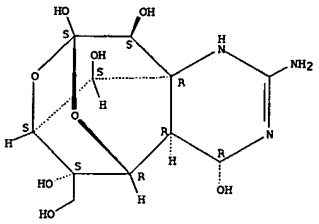
AB Neurodegenerative diseases or disorders are treated by administering a therapeutically effective amount of a compound having anticonvulsant properties which bind to Na channels and modulate the channel without blocking the channel, to prevent irreversible neuronal damage from conditions similar to ischemia. Known N-(2,6-disubstituted phenyl)-N'-3- and 4-pyridinyl ureas and pharmaceutically acceptable acid addition salts thereof, e.g. N-(2-chloro-6-methylphenyl)-N'-4-pyridinyl urea monohydrochloride or N-(2,3-dichlorophenyl)-N'-4-pyridinyl urea, and known anticonvulsant compds., e.g. ralitoline, phenytoin, lamotrigine, tetrodotoxin, lidocaine, and carbamazepine, are used for treating neurodegenerative disorders, perinatal asphyxia, Alzheimer's disease, Huntington's disease, Parkinson's disease, and amyotrophic lateral sclerosis. Treatment with N-(2-chloro-6-methylphenyl)-N'-4-pyridinyl urea provided protection of hippocampal slices from irreversible loss of synaptic potentials after brief application of conditions that mimic ischemia in vitro. N-(2,6-dichlorophenl)-N'-4-pyridinyl urea was prepared from 4-aminopyridine and 2,6-dichlorophenylisocyanate.

IT **4368-28-9**, Tetrodotoxin
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(neurodegenerative diseases and disorders treatment using N-(2,6-disubstituted aromatic)-N'-pyridinyl ureas and other anticonvulsant compds.)

RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L8 ANSWER 91 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)



L8 ANSWER 92 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1990:132107 HCAPLUS
DOCUMENT NUMBER: 112:132107
TITLE: Antiarrhythmic properties of tetrodotoxin against occlusion-induced arrhythmias in the rat: a novel approach to the study of the antiarrhythmic effects of ventricular sodium channel blockade
AUTHOR(S): Abraham, Shlomo; Beatch, Gregory N.; MacLeod, Bernard A.; Walker, Michael J. A.
CORPORATE SOURCE: Fac. Med., Univ. British Columbia, Vancouver, BC, V6T 1W5, Can.
SOURCE: Journal of Pharmacology and Experimental Therapeutics (1989), 251(3), 1166-73
CODEN: JPETAB; ISSN: 0022-3565
DOCUMENT TYPE: Journal
LANGUAGE: English

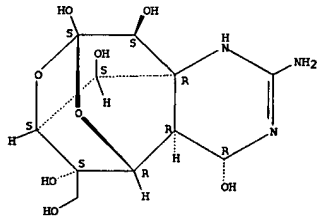
AB Blockade of ventricular sodium conductance (gNa) is believed to play an important role in the beneficial antiarrhythmic effects of class I antiarrhythmic agents. The present study was undertaken to examine the importance of ventricular gNa blockade by assessing the antiarrhythmic profile of tetrodotoxin (TTX), a selective sodium channel blocker. Expts. were performed in pentobarbital-anesthetized and artificially ventilated rats. Two doses of TTX were tested for antiarrhythmic action: a low dose (low TTX, 10 μg/kg of bolus + infusion of 10 μg/kg/h) which blocked only neuronal activity, and a high dose (TTXh, 50 μg/kg of bolus + infusion of 50 μg/kg/h) which also produced signs of ventricular gNa blockade in normal hearts. To control for the decreases in blood pressure and heart rate caused by TTX, hexamethonium, nitroprusside and propranolol were also used. Only TTXh possessed antiarrhythmic activity in rats subjected to myocardial ischemia (produced by ligation of the left anterior descending coronary artery). TTXh reduced dV/dt maximum of the action potential as well as action potential height, and concomitantly prolonged the P-R and QRS intervals of normal hearts. Apparently, drugs which produced hypotension, bradycardia and loss of autonomic function were not antiarrhythmic. On the other hand, the marked antiarrhythmic activity of TTXh appeared to depend upon ventricular gNa blockade. Thus, TTX provides a useful tool for examining the antiarrhythmic properties of ventricular gNa blockade.

IT **4368-28-9**, Tetrodotoxin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(antiarrhythmic activity of, sodium channel blockade in)

RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

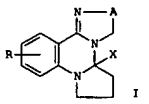
L8 ANSWER 92 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)



L8 ANSWER 93 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1989:515199 HCAPLUS
DOCUMENT NUMBER: 111:115199
TITLE: Preparation, testing, and formulation of heterocyclopyrroloquinazolines as antiarrhythmics
INVENTOR(S): Franke, Albrecht; Ostersehlt, Bernd; Schlecker, Rainer; Rendenbach, Beatrice; Von Philipsborn, Gerda
PATENT ASSIGNEE(S): BASF A.-G., Fed. Rep. Ger.
SOURCE: Ger. Offen., 9 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 3730718	A1	19890323	DE 1987-3730718	19870912
JP 01071881	A2	19890316	JP 1988-222578	19880907
EP 307814	A2	19890322	EP 1988-114755	19880909
EP 307814	A3	19900808		
EP 307814	B1	19920408		
R: AT, BE, CH, DE, ES, FR, GB, IT, LI, NL				
AT 74605	E	19920415	AT 1988-114755	19880909
ES 2032317	T3	19930201	ES 1988-114755	19880909
CA 1331608	A1	19940823	CA 1988-576970	19880909
US 5214047	A	19930525	US 1988-243469	19880912

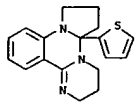
PRIORITY APPLN. INFO.: DE 1987-3730718 A 19870912
EP 1988-114755 A 19880909
OTHER SOURCE(S): CASREACT 111:115199; MARPAT 111:115199
GI



I

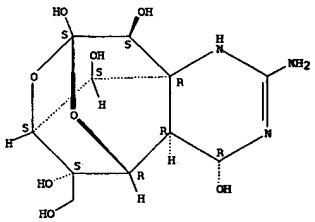
AB The title compds. (I; R = H, halo, OH, NO2, amino, acylamino, C1-4 alkoxy, alkyl, alkylsulfonic acid; A = (C1-4 alkyl-substituted) C1-4 alkylene; X = (substituted) Ph, naphthyl, heterocyclyl] were prepared A mixture of 4-chloro-1-(4-methylphenyl)butane-1-one, 2-(2-aminophenyl)-4,5-dihydroimidazole, NaI, and EtOH were treated with 12 N HCl and the mixture was refluxed for 30 h. The solvent was removed and the residue was heated for 4 h at 120° to give 71% 2,3,5,6,7,8-hexahydro-5-(4-methylphenyl)imidazo[1,2-c]pyrrolo[1,2-a]quinazoline. I prolonged QT times in guinea pigs with ED20's of 0.25-1.5 mg/kg i.v.
IT 122478-34-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic

L8 ANSWER 93 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)
use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of, as antiarrhythmic)
RN 122478-34-6 HCAPLUS
CN 2H-Pyrimido[1,2-c]pyrrolo[1,2-a]quinazoline, 3,4,5a,6,7,8-hexahydro-5a-(2-thienyl)- (9CI) (CA INDEX NAME)



L8 ANSWER 94 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1987:568491 HCAPLUS
DOCUMENT NUMBER: 107:168491
TITLE: Do antiarrhythmic drugs act on the site of abnormal impulse generation or act on the normal myocardium?
AUTHOR(S): Hashimoto, Keitaro; Mitsuhashi, Harumi; Akiyama, Kentaro; Komori, Sadayoshi
CORPORATE SOURCE: Dep. Pharmacol., Yamanashi Med. Coll., Yamanashi, 409-38, Japan
SOURCE: Japanese Circulation Journal (1987), 51(2), 196-202
CODEN: JCIRA2; ISSN: 0047-1828
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Locally-induced digitalis arrhythmia was produced to study whether antiarrhythmic drugs suppress arrhythmia by directly acting on the abnormal impulse generation or by suppressing Na channels of normal myocardium to make it unresponsive to abnormal impulses. Dogs were thoractomized and the anterior descending artery (ADA) was isolated and autoperfused with arterial blood from the carotid artery. Forty μg and an addnl. 10 μg every 20 min of ouabain was injected directly into the ADA produced ventricular tachycardia originating from the digitalis intoxication. Locally injected class 1 antiarrhythmic drugs, including tetrodotoxin, were effective in suppressing this arrhythmia. However, when i.v. applied lidocaine was prevented from reaching the ADA area, lidocaine was not effective in suppressing this arrhythmia. Apparently, class 1 drugs produce antiarrhythmic effect by directly suppressing the digitalis damaged area, not by suppressing the normal myocardium.
IT 4368-28-9, Tetrodotoxin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antiarrhythmic activity of, abnormal impulse generation area vs. normal myocardium as action site of)
RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

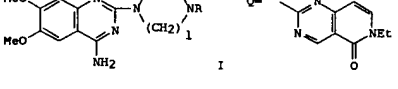
Absolute stereochemistry.



L8 ANSWER 95 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1987:18629 HCAPLUS
DOCUMENT NUMBER: 106:18629
TITLE: 4-Amino-6,7-dimethoxyquinazoline derivatives
INVENTOR(S): Yokoyama, Keiichi; Kato, Koji; Kitahara, Takumi; Ono, Hiroyasu; Nishina, Takashi; Kumakura, Mikio; Awaya, Akira; Nakano, Takuo
PATENT ASSIGNEE(S): Mitsui Petrochemical Industries, Ltd., Japan; Mitsui Pharmaceuticals, Inc.
SOURCE: Jpn. Kokai Tokkyo Koho, 56 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 61140568	A2	19860627	JP 1984-263015	19841214
JP 05028709	B4	19930427		
US 4734418	A	19880329	US 1985-805905	19851206
CA 1307786	A1	19920922	CA 1985-497106	19851206
EP 188094	A2	19860723	EP 1985-309049	19851212
EP 188094	A3	19871223		
EP 188094	B1	19920318		
R: DE, FR, GB, IT				
HU 42479	A2	19870728	HU 1985-4783	19851213
HU 198481	B	19891030		

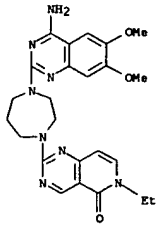
PRIORITY APPLN. INFO.: JP 1984-263015 A 19841214
JP 1985-194968 A 19850905
JP 1985-204463 A 19850918
OTHER SOURCE(S): CASREACT 106:18629
GI



I

AB The title compds. (I; R = heterocyclyl; R1 = H, MeO; l = 2, 3), useful as antihypertensives, were prepared Thus, a mixture of 4-amino-2-chloro-6,7-dimethoxyquinazoline and 5,6-dihydro-6-ethyl-5-oxo-2-piperazinopyrido[4,3-d]pyrimidine in Me2CHCH2CH2OH containing Et3N was refluxed for 4 h to give 83%
I (R = Q; R1 = H; l = 2). I at 1 mg/kg p.o. lowered the blood pressure in spontaneously hypertensive rats. Tablets containing I were prepared
IT 104965-69-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of, as antihypertensive)
RN 104965-69-7 HCAPLUS
CN Pyrido[4,3-d]pyrimidin-5(6H)-one, 2-[4-(4-amino-6,7-dimethoxy-2-

L8 ANSWER 95 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)
quinazolinyl)hexahydro-1H-1,4-diazepin-1-yl]-6-ethyl- (9CI) (CA INDEX NAME)



L8 ANSWER 96 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1986:608919 HCAPLUS
DOCUMENT NUMBER: 105:208919
TITLE: Quinazoline derivatives and antihypertensive preparations containing them
INVENTOR(S): Yokoyama, Keiichi; Kato, Koji; Kitahara, Takumi; Ohno, Hiroyasu; Nishina, Takashi; Awaya, Akira; Nakano, Takuo; Watanabe, Kazuyuki; Saruta, Sakae; Kumakura, Mikio
PATENT ASSIGNEE(S): Mitsui Petrochemical Industries, Ltd., Japan; Mitsui Pharmaceuticals, Inc.
SOURCE: Eur. Pat. Appl., 235 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

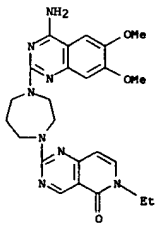
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 188094	A2	19860723	EP 1985-309049	19851212
EP 188094	A3	19871223		
EP 188094	B1	19920318		
R: DE, FR, GB, IT				
JP 61140568	A2	19860627	JP 1984-263015	19841214
JP 05028709	B4	19930427		
JP 62056488	A2	19870312	JP 1985-194968	19850905
JP 03071430	B4	19911113		
JP 62067077	A2	19870326	JP 1985-204463	19850918
JP 05029223	B4	19930428		

PRIORITY APPLN. INFO.: JP 1984-263015 A 19841214
JP 1985-194968 A 19850905
JP 1985-204463 A 19850918
OTHER SOURCE(S): CASREACT 105:208919; MARPAT 105:208919
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

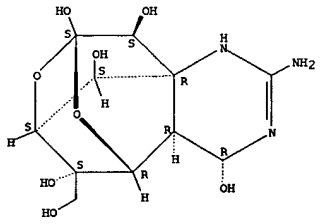
AB Piperazinyl- and homopiperazinylquinazolines I (R1 = H, MeO; R2, R3 = H, alkoxy; R4 = H, NH2; R5 = substituted 2-pyrimidinyl, 2-pyridinyl, 2-quinolinyl, fused pyrimidinyl; n = 2, 3) were prepared as antihypertensives. Thus, 4-benzyl-1-piperazinecarboxamidine sulfate was cyclocondensed with MeCOC(CO2Me):CHOMe to give pyrimidinecarboxylate II. This was amidated with EtNH2 and cyclocondensed with DMF to give pyridopyrimidinone III, which was debenzylated and condensed with 4-amino-2-chloro-6,7-dimethoxyquinazoline to give piperazinylquinazoline IV. In rats 1 mg IV/kg orally reduced blood pressure 23.0% after 6 h, the effect lasting 24 h. Tablets were prepared each containing I 1, starch 60, microcrystn. cellulose 35, light silica 3, and Mg stearate 1 mg.
IT **104965-69-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of, as antihypertensive)

L8 ANSWER 96 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)
RN 104965-69-7 HCAPLUS
CN Pyrido[4,3-d]pyrimidin-5(6H)-one, 2-[4-(4-amino-6,7-dimethoxy-2-quinazolinyl)hexahydro-1H-1,4-diazepin-1-yl]-6-ethyl- (9CI) (CA INDEX NAME)



L8 ANSWER 97 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1985:142963 HCAPLUS
DOCUMENT NUMBER: 102:142963
TITLE: Role of tetrodotoxin-sensitive ion channels in evolvement and cessation of cardiac arrhythmia due to myocardial ischemia
AUTHOR(S): Rozenshtraukh, L. V.; Anyukhovskii, E. P.; Sharov, V. G.
CORPORATE SOURCE: USSR Cardiol. Res. Cent., Moscow, USSR
SOURCE: Cardiol.: Int. Perspect., [Proc. World Congr.], 9th (1984), Meeting Date 1982, Volume 2, 955-70. Editor(s): Chazov, E. I.; Smirnov, V. N.; Oganov, R. G. Plenum: New York, N. Y.
CODEN: 53HTA8
DOCUMENT TYPE: Conference
LANGUAGE: English
AB Tetrodotoxin (I) [4368-28-9] showed antiarrhythmic activity in dogs with arrhythmia induced by coronary artery ligation at 2 μg/kg i.v., as well as in isolated hearts from dogs 24 h after coronary artery occlusion (i.e. during the late stage of infarction) at 4 + 10-8 g/mL. I also potentiated the antiarrhythmic activity of ethmozine [29560-58-5] and mexiletine [31828-71-4] in vivo.
IT **4368-28-9**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antiarrhythmic activity of)
RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L8 ANSWER 98 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1985:4046 HCAPLUS
DOCUMENT NUMBER: 102:4046
TITLE: Cyclic AMP-arrhythmias: induction and inhibition
AUTHOR(S): Podzuweit, T.; Binz, K. H.; Schaper, W.
CORPORATE SOURCE: Max-Planck-Inst. Physiol. Clin. Res., Bad Nauheim, D-6350, Fed. Rep. Ger.
SOURCE: Recent Advances in Cardiac Arrhythmias (1983), 1, 1-8
CODEN: RACAEX; ISSN: 0951-807X
DOCUMENT TYPE: Journal
LANGUAGE: English

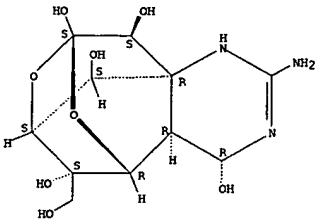
AB Ventricular arrhythmias were induced in the intact nonischemic pig heart, by slow subepicardial infusion (10 μL/min) of agents known to increase myocardial cAMP. Arrhythmias could be induced by infusing 1 of the following agents, dissolved in 2.5 mM CaCl2-150 mM NaCl: noradrenaline (NA), adrenaline 10-5M each; isoproterenol-10-6 M; N6,O2-dibutyryl-cAMP, N6-monobutyryl-cAMP 5.10-2M each; 8-Br-cAMP-5.10-2M together with Ro 7-2956-5.10-4M. In the presence of myocardial ischemia arrhythmias could also be induced by infusing caffeine, theophylline-5.10-2M; histamine, glucagon, or dopamine-10-3M each. Other agents precipitating arrhythmias were ouabain-10-5M and aconitine-10-6M. Prolonged infusion of the latter resulted in ventricular fibrillation. The induction of ventricular tachycardia (VT) by NA infusion was facilitated by simultaneously infusing Ca2+. The NA-Ca2+-VT could be abolished by the resp. infusion of pindolol-10-6M; propanolol-10-4M; verapamil, D 600-10-4M each; MnCl2-5.10-4M; NiCl2, CoCl2-2.5.10-3M each; acetylcholine, butyrylcholine-10-4M each; carbamylcholine, methacholine-10-6M each; bethanechol-10-5M or muscarine-10-6M. Biochem. anal. showed that cAMP was increased at the NA-Ca2+-infusion site when arrhythmias ensued and that both β-blockers and choline esters prevent such accumulation of cAMP. During VT induced by NA-Ca2+-infusion tachycardia was stopped within 10-30 s by occluding the coronary artery supplying the infusion area. This ischemic effect was readily reversed by coronary reperfusion. Infusion of NA-Ca2+ outside the ischemic area (anterior descending coronary artery ligated 2-thirds of the way from its origin) consistently precipitated ventricular fibrillation within 6 min after coronary artery ligation. Myocardial cAMP mediates the effects on heart rhythm of adrenergic overstimulation and muscarinic receptor activation by modulating the slow Ca2+ inward current, preferably by non-ischemic or reperfused myocardium.

IT **4368-28-9**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(antiarrhythmic activity of, cAMP in relation to)

RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L8 ANSWER 98 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)



L8 ANSWER 99 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN

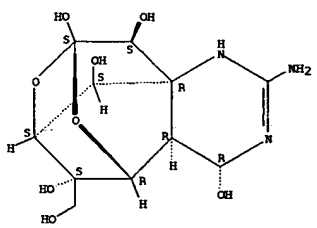
ACCESSION NUMBER: 1984:17436 HCAPLUS
DOCUMENT NUMBER: 100:17436
TITLE: Comparative effects of fast- and slow-ion channel blocking agents on reperfusion-induced arrhythmias in the isolated perfused rat heart
AUTHOR(S): Winslow, E.; Marshall, R. J.; Hope, F. G.
CORPORATE SOURCE: Sci. Dev. Group, Organon Lab. Ltd., Newhouse/Lanarkshire, ML1 5SH, UK
SOURCE: Journal of Cardiovascular Pharmacology (1983), 5(6), 928-36
CODEN: JCPCDT; ISSN: 0160-2446
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The effects of bepridil [64706-54-3] (1-4 μM), a new antianginal agent, on reperfusion-induced arrhythmias (RA) in the isolated perfused rat heart were compared with those of tetrodotoxin [4368-28-9] (0 16-1.57 μM), verapamil [52-53-9] (0.5-2 μM), diltiazem [42399-41-7] (1-2 μM), nifedipine [21829-25-4] (0.02-0.2 μM) and nitrendipine [39562-70-4] (0.02-0.2 μM). In comparable neg. inotropic concns., neither nifedipine nor nitrendipine reduced the incidence of RA, whereas the other 4 agents did. Protection against RA does not appear to be related to coronary vasodilatation or to a reduction in the degree of ischemia as assessed by lactate dehydrogenase release. However, neg. chronotropism appears to be relevant in the mechanism of action of the Ca antagonists. Substantial protection against RA by all active drugs was associated with PR prolongation and(or) atrioventricular block or suppression of sinus rhythm. Thus, bradycardia may play an important role in the antiarrhythmic action of bepridil, but the relative contributions made by inhibition of the inward Ca and(or) Na currents remain unclear.

IT **4368-28-9**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(antiarrhythmic activity of)

RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

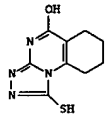


L8 ANSWER 99 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)

L8 ANSWER 100 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1977:50802 HCAPLUS
DOCUMENT NUMBER: 86:50802
TITLE: Preventing metastasis and primary tumor growth of H. Ep. Number 3
INVENTOR(S): Shen, Ysung-Ying; Gitterman, Charles O.
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: U.S., 3 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 3991192	A	19761109	US 1975-600554	19750731
PRIORITY APPLN. INFO.:			US 1974-467239	A2 19740506

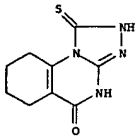
GI



I

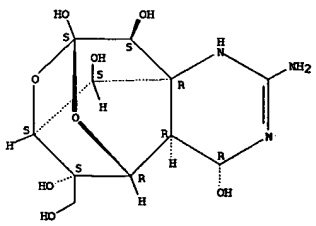
AB 1-Mercapto-5-hydroxy-6,7-tetramethylene-s-triazolo[3,4-b]pyrimidine (I) [61413-52-3] prevents in ovo metastasis of human epidermoid carcinoma and exhibits antitumor activity against primary human epidermoid carcinoma and other tumors, such as adenocarcinoma and sarcoma. Dosage units containing 100-500 mg I were recommended.
IT **61413-52-3**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(neoplasm inhibitor)
RN 61413-52-3 HCAPLUS
CN [1,2,4]Triazolo[4,3-a]quinazolin-5(1H)-one, 2,3,6,7,8,9-hexahydro-1-thioxo- (9CI) (CA INDEX NAME)

L8 ANSWER 100 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)



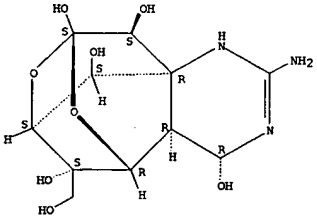
L8 ANSWER 101 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1976:516725 HCAPLUS
DOCUMENT NUMBER: 85:116725
TITLE: The local anesthetic activity of tetrodotoxin alone and in combination with vasoconstrictors and local anesthetics
AUTHOR(S): Adams, H. Jack; Blair, Murray R., Jr.; Takman, Bertil H.
CORPORATE SOURCE: Res. Dep., Astra Pharm. Prod., Inc., Framingham, MA, USA
SOURCE: Anesthesia & Analgesia (Baltimore, MD, United States) (1976), 55(4), 568-73
CODEN: AACRAT; ISSN: 0003-2999
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Tetrodotoxin (TTX) [4368-28-9], alone and in combination with various vasoconstrictors and local anesthetics, was evaluated for its ability to produce peripheral nerve blocks in the rat and central neural block in the cat and dog. High frequency and long duration of block were attained if sufficiently high concns. of TTX were used, although latency was long and high dosage produced systemic toxicity. Frequency and mean duration of block could be increased and systemic toxicity reduced if TTX was administered with a vasoconstrictive agent. Conventional local anesthetics also enhanced the nerve-blocking activity of TTX. When appropriate concns. of TTX and local anesthetics were used, a high frequency of blocks characterized by short latency and long duration were demonstrated. Some indirect evidence that local anesthetics enhance TTX activity by reversibly increasing the permeability of various neural barriers to TTX is presented.
IT **4368-28-9**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anesthetic activity of, local anesthetics and vasoconstrictors effect on)
RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



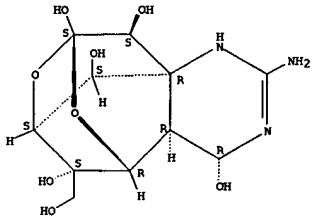
L8 ANSWER 102 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1972:429843 HCAPLUS
DOCUMENT NUMBER: 77:29843
TITLE: Pharmacology of tetrodotoxin and saxitoxin
AUTHOR(S): Kao, C. Y.
CORPORATE SOURCE: Downstate Med. Cent., State Univ. New York, Brooklyn, NY, USA
SOURCE: Federation Proceedings (1972), 31(3), 1117-23
CODEN: FEPRA7; ISSN: 0014-9446
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 35 refs. Tetrodotoxin (I) [4368-28-9] and saxitoxin (II) [35523-89-8] although chemical different, interfered with the early transiently open ionic channel through which Na [7440-23-5] ions pass in most common excitable membranes. A synthetic guanidinium compound bearing partial structural similarity to I resembled I qual. in having some selective actions on the spike-generating process of the frog sartorius muscle. This qual. resemblance supported the idea that the guanidinium moiety was important for the actions of I. In whole animals, I and II caused severe hypotension. II was a weaker hypotensive than I, and produced a late pressor effect that was due to catechol amine secretion.
IT **4368-28-9**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmacology of)
RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



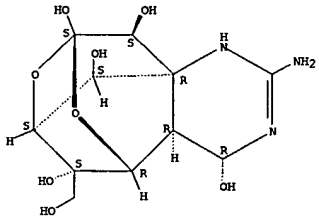
L8 ANSWER 103 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1971:110240 HCAPLUS
DOCUMENT NUMBER: 74:110240
TITLE: Effect of saline infusion on the respective antiarrhythmic effects of imipramine and tetrodotoxin against aconitine-induced arrhythmias in the rat
AUTHOR(S): Lagier, Georges; Auclair, Marie C.; Lechat, Paul
CORPORATE SOURCE: Inst. Pharmacol., Ec. Med., Paris, Fr.
SOURCE: Therapie (1971), 26(1), 109-19
CODEN: THERAP; ISSN: 0040-5957
DOCUMENT TYPE: Journal
LANGUAGE: French
GI For diagram(s), see printed CA Issue.
AB Infusion of hypertonic NaCl solns. (1.5-4.5%) in anesthetized, artificially ventilated rats suppressed the antiarrhythmic effects of tetradotoxin (I) against aconitine-induced arrhythmias, but had no such effect on the antiarrhythmic activity of imipramine (II). It was suggested that the antagonistic effect of Na+ with I occurred in the myometrium, and that the absence of such an antagonism with II mayhave been due to strong tissue binding of II.
IT **4368-28-9**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(antiarrhythmic activity of, sodium chloride effect of)
RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



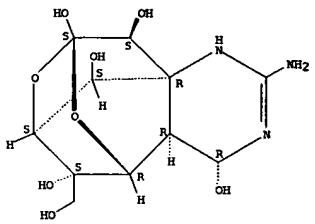
L8 ANSWER 104 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1970:475367 HCAPLUS
DOCUMENT NUMBER: 73:75367
TITLE: Suppression of the antiarrhythmic effect of tetrodotoxin against aconitine in rat by perfusion of hypertonic sodium chloride
AUTHOR(S): Lagier, Georges; Auclair, Marie C.; Lechat, Paul
CORPORATE SOURCE: Inst. Pharmacol., U.E.R. Biomed. Cordeliers, Paris, Fr.
SOURCE: Comptes Rendus des Seances de l'Academie des Sciences, Serie D: Sciences Naturelles (1970), 270(26), 3325-8
CODEN: CHDDAT; ISSN: 0567-655X
DOCUMENT TYPE: Journal
LANGUAGE: French
AB Perfusion of a hypertonic NaCl (15-45%) solution into anesthetized, artificially ventilated rats suppressed the antiarrhythmic effect of tetrodotoxin against aconitine nitrate-induced cardiac arrhythmias. This effect was due to Na since perfusion of hypertonic glucose solns. was devoid of this activity.
IT **4368-28-9**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(antiarrhythmic activity of, hypertonic sodium chloride antagonism of)
RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



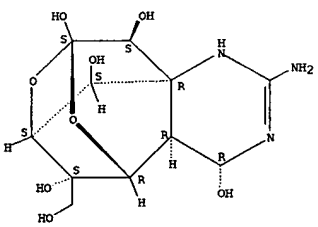
L8 ANSWER 105 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1969:437457 HCAPLUS
DOCUMENT NUMBER: 71:37457
TITLE: Pharmacologic effects of tetrodotoxin; cardiovascular and antiarrythmic activities
AUTHOR(S): Bernstein, Martin E.
CORPORATE SOURCE: Indiana Univ., Bloomington, IN, USA
SOURCE: (1968) 125 pp. Avail.: 69-4728
From: Diss. Abstr. B 1969, 29(9), 3422
DOCUMENT TYPE: Dissertation
LANGUAGE: English
AB Unavailable
IT **4368-28-9**
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(pharmacology of)
RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L8 ANSWER 106 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1968:494968 HCAPLUS
DOCUMENT NUMBER: 69:94968
TITLE: Comparative pharmacological actions of ciguatoxin and tetrodotoxin, a preliminary account
AUTHOR(S): Ogura, Yasumi; Nara, Junko; Yoshida, Tamao
CORPORATE SOURCE: Dep. Toxicol. Pharmacol., Chiba Univ., Chiba, Japan
SOURCE: Toxicon (1968), 6(2), 131-40
CODEN: TOXIA6; ISSN: 0041-0101
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The pharmacol. actions of a MeOH-soluble extract of ciguatoxin from Lutjanus bohar were compared with those previously reported for crystalline tetrodotoxin in crayfish, mice, and rats. In mice, there were no significant differences in median lethal dosages (LD50) of i.p. (560 mg./kg.) or orally (530 mg./kg.) administered ciguatoxin. The LD50 for intracaudally administered ciguatoxin was 29.3 mg./kg. in crayfish. In rats, injected ciguatoxin (10-30 mg./kg.) depressed blood pressure, and this was accompanied by respiratory failure. In mice, ciguatoxin did not show physostigmine-like action on electroencephalograms. Progressively higher doses of ciguatoxin (500-1000 mg./kg., i.p.) depressed heart rate, and evoked arrhythmia and bradycardia followed by death of rats. Ciguatoxin and tetrodotoxin produced similar toxic symptoms, but there seemed to be qual. pharmacol. differences between them.
IT **4368-28-9**
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(pharmacology of, ciguatoxin in relation to)
RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L8 ANSWER 107 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1968:409494 HCAPLUS
DOCUMENT NUMBER: 69:9494
TITLE: Mechanism of local anesthetic action of crystalline tetrodotoxin and its derivatives
AUTHOR(S): Ogura, Yasumi; Mori, Yoko
CORPORATE SOURCE: Dep. Toxicol. Pharmacol., Chiba Univ., Chiba, Japan
SOURCE: European Journal of Pharmacology (1968), 3(1), 58-67
CODEN: EJPHAZ; ISSN: 0014-2999
DOCUMENT TYPE: Journal
LANGUAGE: English

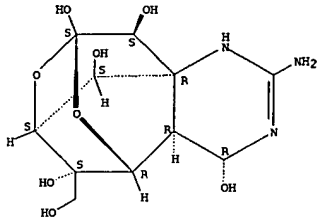
AB The local anesthetic actions of intradermally given tetrodotoxin, anhydrotetrodotoxin (AHT), monoformylanhydrotetrodotoxin (MFAHT), deoxytetrodotoxin (DOT), methoxytetrodotoxin (MOT), ethoxytetrodotoxin (EOT), tetrodoaminotoxin (TAT), diacetylanhydrotetrodotoxin (DAAHT), and tetrodonic acid were tested in mice (0.011-58.2 mg./kg.), guinea pigs (7.5 + 10-5-7.8 + 10-1mM) and rabbits, and on desheathed crayfish abdominal nerve fibers (3 tme 10-7-3 + 10-1 μM) and compared with the effects of procaine and dibucaine. Of all the compds. tested, the crayfish nerve fibers were most sensitive to the anesthetic action of tetrodotoxin. In alkaline solution tetrodotoxin was more effective in the sheathed nerve preparation and in neutral solution it was more effective in the desheathed nerve. This suggests that the active form is the cationic form of tetrodotoxin and it penetrates nerve tissue more rapidly as its uncharged form. Heating a tetrodotoxin solution at alkaline pH greatly decreased its activity, whereas the same treatment at acidic pH did not alter its activity. Its activity was not influenced by 10% glucose, 5% taurine, 1% hyaluronic acid, 10% dextrin, or 1% serum albumin. All the tetrodotoxin derivs. tested showed local anesthetic activity, although they were lower than that of the parent compound It is suggested that hydrophobic and H bonding may be involved in the binding mechanism of tetrodotoxin, whereas the lack of a hemilactal ring form and the formation of an ether linkage between C atoms C-9 and C-4 may induce the lowering of local anesthetic activity. 21 references.

IT **4368-28-9**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(anesthetic activity of)

RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L8 ANSWER 107 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)



L8 ANSWER 108 OF 108 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1967:489145 HCAPLUS
DOCUMENT NUMBER: 67:89145
TITLE: Structure and activity in tetrodotoxin derivatives
AUTHOR(S): Deguchi, Takehiko
CORPORATE SOURCE: Med. Lab. Pharmacol. Central Res. Lab., Sankyo Co., Tokyo, Japan
SOURCE: Japanese Journal of Pharmacology (1967), 17(2), 267-78
CODEN: JJPAAZ; ISSN: 0021-5198
DOCUMENT TYPE: Journal
LANGUAGE: English

GI For diagram(s), see printed CA Issue.

AB Pharmacol. properties of compds. structurally related to the neurotoxin, tetrodotoxin (I, R = OH), were studied. All the compds., including tetrodotoxin, deoxytetrodotoxin (I, R = H), methoxytetrodoxotin (I, R = OMe), ethoxytetrodotoxin (I, R = OEt), tetrodaminotoxin (I, R = NH2), anhydrotetrodotoxin (II, R1 = R2 = H), 11-monoformylanhydrotetrodotoxin formate (II, R1 = H, R2 = CHO), 6,11-diacetylanhydrotetrodotoxin (II, R1 = R2 = Ac), and tetrodonic acid (III), showed similar pharmacol. properties in symptomatology in mice, blood pressure and respiration expts. in cats, and in tests on nerve conduction-blocking activity in the frog sciatic nerve and on spasmolytic activity in the guinea pig ileum. A comparison of the quant. differences in the pharmacol. activity of the compds. showed that neurotoxin activity depended on the integrity of the hemilactal structure and OH groups in positions 4 and 9 and either or both of these in positions 6 and 11.

IT **4368-28-9**
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(pharmacology of)

RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.